



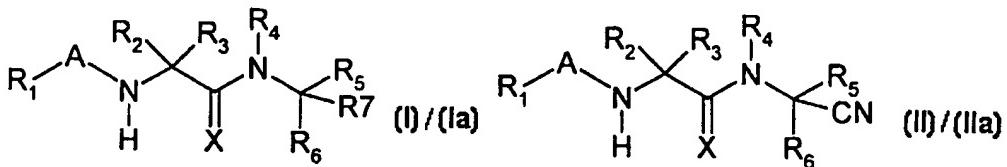
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(54) Title: COMPOUNDS USEFUL AS REVERSIBLE INHIBITORS OF CATHEPSIN S



(57) Abstract

Disclosed are novel cathepsin S reversible inhibitory compounds of formulas (I),(Ia) and (II),(IIa) as defined herein. The compounds are useful for treating autoimmune diseases. Also disclosed are processes for making such novel compounds.

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COMPOUNDS USEFUL AS REVERSIBLE INHIBITORS OF CATHEPSIN S**RELATED APPLICATIONS**

The benefit of prior provisional application Serial Number 60/122,570, filed on March 2,
5 1999, is hereby claimed.

TECHNICAL FIELD OF THE INVENTION

This invention relates to peptidyl cysteine protease inhibitors. The compounds are
10 reversible inhibitors of the cysteine protease cathepsin S and are therefore useful in the
treatment of autoimmune diseases. The invention also relates to processes for preparing
such compounds and pharmaceutical compositions comprising them.

BACKGROUND OF THE INVENTION

15

Cathepsin S is a member of the papain family, within the papain superfamily of cysteine
proteases. The papain family is the largest group of cysteine proteases and includes
proteases such as cathepsins B, H, K, L, O and S. (A.J. Barrett et al., 1996, Perspectives
in Drug Discovery and Design, 6, 1). The cysteine proteases have important roles in
20 human biology and diseases including atherosclerosis, emphysema, osteoporosis, chronic
inflammation and immune disorders (H.A. Chapman et al., 1997, Ann. Rev. Physiol., 59,
63). Cathepsin S plays a key role in regulating antigen presentation and immunity (H.A.
Chapman, 1998, Current Opinion in Immunology, 10, 93; R. J. Riese et al., 1998, J. Clin.
Invest., 101, 2351; R.J. Riese et al., 1996, Immunity, 4, 357).

25

The specificity of the immune response relies on processing of foreign protein and
presentation of antigenic peptide at the cell surface. Antigenic peptide is presented bound
to MHC Class II, a heterodimeric glycoprotein expressed in certain antigen presenting
cells of hematopoietic lineage, such as B cells, macrophages and dendritic cells.
30 Presentation of antigen to effector cells, such as T-cells, is a fundamental step in
recognition of non-self and thus initiation of the immune response.

Recently MHC Class II heterodimers were shown to associate intracellularly with a third molecule designated invariant chain. Invariant chain facilitates Class II transport to the endosomal compartment and stabilizes the Class II protein prior to loading with antigen.

- 5 Invariant chain interacts directly with Class II dimers in the antigen-binding groove and therefore must be proteolyzed and removed or antigen cannot be loaded or presented. Current research suggests that invariant chain is selectively proteolyzed by cathepsin S, which is compartmentalized with MHC Class II complexes within the cell. Cathepsin S degrades invariant chain to a small peptide, termed CLIP, which occupies the antigen –
10 binding groove. CLIP is released from MHC Class II the interaction MHC Class II with HLA-DM, a MHC-like molecule thus freeing MHC Class II to associate with antigenic peptides. MHC Class II-antigen complexes are then transported to the cell surface for presentation to T-cells, and initiation of the immune response.

Cathepsin S, through proteolytic degradation of invariant chain to CLIP, provides a
15 fundamental step in generation of an immune response. It follows that inhibition of antigen presentation via prevention of invariant chain degradation by cathepsin S could provide a mechanism for immuno-regulation. Control of antigen-specific immune responses has long been desirable as a useful and safe therapy for autoimmune diseases. Such diseases include Crohn's disease and arthritis, as well as other T-cell-mediated
20 immune responses (C. Janeway and P. Travers, 1996, Immunobiology, The Immune System in Health and Disease, Chapter 12). Furthermore, cathepsin S, which has broad pH specificity, has been implicated in a variety of other diseases involving extracellular proteolysis, such as Alzheimer's disease (U. Muller-Ladner et al., 1996, Perspectives in Drug Discovery and Design, 6, 87) and atherosclerosis (G.K. Sukhova et al., 1998, J.
25 Clin. Invest., 102, 576).

Cysteine proteases are characterized by having a cysteine residue at the active site which serves as a nucleophile. The active site also contains a histidine residue. The imidazole ring on the histidine serves as a base to generate a thiolate anion on the active site
30 cysteine, increasing its nucleophilicity. When a substrate is recognized by the protease, the amide bond to be cleaved is directed to the active site, where the thiolate attacks the

carbonyl carbon forming an acyl-enzyme intermediate and cleaving the amide, liberating an amine. Subsequently, water cleaves the acyl-enzyme species regenerating the enzyme and liberating the other cleavage product of the substrate, a carboxylic acid.

- 5 A proposed mechanism of action of the cysteine protease inhibitors of this invention is that the inhibitors contain a functionality that can react (reversibly or irreversibly) with the active site cysteine. The reactive functionality is attached to a peptide or peptide mimic that can be recognized and accommodated by the region of the protease surrounding the active site. The nature of both the reactive functionality and the
10 remaining portion of the inhibitor determine the degree of selectivity and potency toward a particular protease.

Examples of reactive functionalities that have been described (D. Rasnick, 1996, Perspectives in Drug Discovery and Design, 6, 47) on cysteine protease inhibitors include
15 peptidyl diazomethanes, epoxides, monofluoroalkanes and acyloxymethanes, which irreversibly alkylate the cysteine thiol. Other irreversible inhibitors include Michael acceptors such as peptidyl vinyl esters and other carboxylic acid derivatives (S. Liu et al., J. Med Chem., 1992, 35, 1067) and vinyl sulfones (J.T. Palmer et al., 1995, J. Med Chem., 38, 3193).

20 Reactive functionalities that form reversible complexes with the active site cysteine include peptidyl aldehydes (R.P. Hanzlik et al., 1991, Biochim. Biophys. Acta., 1073, 33), which are non-selective, inhibiting both cysteine and serine proteases as well as other nucleophiles. Peptidyl nitriles (R.P. Hanzlik et al., 1990, Biochim. Biophys. Acta., 1035, 25 62) are less reactive than aldehydes and therefore more selective for the more nucleophilic cysteine proteases. Various reactive ketones have also been reported to be reversible inhibitors of cysteine proteases (D. Rasnick, 1996, ibid). In addition to reacting with the nucleophilic cysteine of the active site, reactive ketones may react with water, forming a hemiketal which may act as a transition state inhibitor.

30

Examples of cathepsin S inhibitors have been reported previously. J.T. Palmer (U.S 5,776,718, 1998) described reversible peptidyl sulfones as inhibitors of cysteine proteases including cathepsin S. J.L. Klaus et al. (WO 9640737, 1996) described reversible inhibitors of cysteine proteases including cathepsin S, containing an ethylene diamine.

5

Additional peptidyl nitriles or peptidyl ketoheterocycles have been reported either as protease inhibitors or as having other utilities. For example, both nitriles and keto-heterocycles are described by B.A. Rowe et al. (US 5714471, 1998) as protease 10 inhibitors useful in the treatment of neurodegenerative diseases. Peptidyl nitriles are reported by B. Malcolm et al. (WO 9222570, 1992) as inhibitors of picornavirus protease. H. Saika et al. (WO 9512611, 1995) report peptidyl nitriles among compounds having endothelin receptor antagonist activity. B.J. Gour-Salin (Can. J. Chem., 1991, 69, 1288) and T.C. Liang (Arch. Biochim. Biophys., 1987, 252, 626) described peptidyl nitriles as 15 inhibitors of papain. D.W. Woolley et al. (J. Org. Chem., 1963, 28, 2012) described a peptidyl nitrile as a chemical intermediate.

Peptidyl ketoheterocycles having protease inhibiting or other activities have been reported, include inhibitors of serine proteases described by R. D. Tung et al. (WO 20 9817679, 1998). Inhibitors of Factor X_a have been described by C.K. Marlowe et al. (WO 9640744, 1996). Peptidyl ketoheterocycles useful in the treatment of thrombin related diseases have been described by M. Costanzo et al. (WO 9640742, 1996).

A reversible inhibitor presents a more attractive therapy than irreversible inhibitors. Even 25 compounds with high specificity for a particular protease can bind non-target enzymes. An irreversible compound could therefore permanently inactivate a non-target enzyme, increasing the likelihood of toxicity. Furthermore, any toxic effects resulting from inactivation of the target enzyme would be mitigated by reversible inhibitors, and could be easily remedied by modified or lower dosing. Finally, covalent modification of an 30 enzyme by an irreversible inhibitor could potentially generate an antibody response by acting as a hapten.

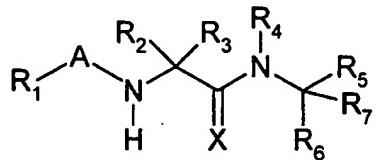
In light of the above, there is a clear need for compounds which reversibly and selectively inhibit cathepsin S, such inhibitors would be useful in therapy for antigen-specific immune responses as well as for indications in which cathepsin S exacerbates disease
 5 through extracellular activity.

BRIEF DESCRIPTION OF THE INVENTION

The work cited above supports the principle that inhibition of cathepsin S and subsequent inhibition of antigen presentation will be beneficial in the treatment of various disease
 10 states. It is therefore an object of this invention to provide novel compounds that inhibit antigen presentation by virtue of reversible inhibition of the cysteine protease cathepsin S. It is a further object of the invention to provide methods for treating diseases and pathological conditions involving immune disorders such as rheumatoid arthritis. It is yet a further object of the invention to provide processes for preparation of the above-
 15 mentioned novel compounds.

DETAILED DESCRIPTION OF THE INVENTION

The invention provides novel compounds of the formula (I):



20

(I)

25

A is -C(Y)- or -SO2-

Y is O, S or NR_a wherein R_a is selected from the group consisting of H, alkyl, aryl, alkoxy, aryloxy, alkylamino and arylamino;

30

R₁ is alkyl, cycloalkyl, aryl, heterocycll, heteroaryl or amino wherein R₁ is optionally substituted by one or more R_b;

- 5 R_b is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocycll, heteroaryl, alkoxy, aryloxy, alkoxy carbonyl, aryloxy carbonyl, alkanoyl, aroyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocycll or heteroaryl, alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocycll or heteroaryl, alkoxy carbonylamino, aryloxy carbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocycll or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R_b may be further optionally substituted by one or more R_c;
- 20 R_c is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocycle, heteroaryl, arylalkyl, alkoxy, aryloxy, arylalkoxy, alkanoyl, aroyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocycll or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

25 R₂ is H or alkyl;

R₃ is H, alkyl, cycloalkyl, aryl, heterocycll or heteroaryl, wherein R₃ is optionally substituted by one or more groups of the formula R_d;

- 30 R_d is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocycll, heteroaryl, alkoxy, aryloxy, arylalkoxy, alkoxy carbonyl, aryloxy carbonyl, alkanoyl, aroyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocycll or heteroaryl, alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocycll or heteroaryl, alkoxy carbonylamino, aryloxy carbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocycll or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R_d may be further optionally substituted by one or more R_e;

R_e is selected from the group consisting of alkyl, cycloalkyl, aryl, arylalkyl, alkoxy, aryloxy, arylalkoxy, alkanoyl, aroyl, amino, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

5

R₄ is H or alkyl;

10 R₅ is H, alkyl or cycloalkyl;

R₆ is H, alkyl, cycloalkyl, aryl, heterocyclyl or heteroaryl, wherein R₆ is optionally substituted by one or more groups of the formula R_f;

15

R_f is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkoxy, aryloxy, alkanoyl, aroyl, arylalkoxy, heteroarylalkoxy, alkoxy carbonyl, aryloxy carbonyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylalkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkoxy carbonylamino, aryloxy carbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R_f may be further optionally substituted by one or more R_g;

30

R_g is selected from the group consisting of alkyl, cycloalkyl, aryl optionally substituted by halogen, C₁-5alkyl or C₁-5alkoxy, heterocyclyl, heteroaryl, alkoxy, aryloxy, arylalkoxy, alkoxy carbonyl, aryloxy carbonyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl; alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl; alkoxy carbonylamino, aryloxy carbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl; halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

or R₅ together with R₆ form a 3 to 6 membered carbocyclic ring, the carbocyclic ring being optionally substituted with one or more R_h;

- 5 R_h is selected from the group consisting of alkyl, aryl, alkoxy carbonyl, aryloxy carbonyl, arylalkoxy carbonyl, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with a group selected from alkyl, cycloalkyl, aryl, arylalkyl, heterocyclyl or heteroaryl; halogen, hydroxy, carboxy and cyano;
- 10 R₇ is R₈-C(Z)-;
- 15 wherein Z is O, S, or NR_i wherein R_i is selected from the group consisting of H, alkyl, aryl, alkoxy, aryloxy and hydroxy;
- 20 R₈ is a 5-8 membered monocyclic heteroaryl or 8-11 membered bicyclic heteroaryl ring system, each of the monocyclic or bicyclic ring systems having 1-4 of the same or different heteroatoms selected from the group consisting of N, O and S wherein any of the above R₈ can be optionally substituted by one or more R_j;
- 25 R_j is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, arylalkyl, alkoxy, aryloxy, alkanoyl, aroyl, arylalkoxy, alkoxy carbonyl, aryloxy carbonyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylalkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl; alkoxy carbonylamino, aryloxy carbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl; halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R_j may be further optionally substituted by one or more R_k;
- 35 R_k is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkoxy, aryloxy, arylalkoxy, alkoxy carbonyl, aryloxy carbonyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkoxy carbonylamino, aryloxy carbonylamino, arylalkoxy carbonylamino, arylaminosulfonyl, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein
- 40 45

the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

- 5 X is O, S or N-OH;
and the pharmaceutically acceptable derivatives thereof;

with the proviso that when R₆ is alkyl the alkyl must be substituted with R_f wherein R_f is not hydroxy, sulfhydryl or halogen.

10

Preferred compounds of the formula (I) are those wherein:

- 15 R_a is selected from the group consisting of H, alkyl and aryl;

20 R₁ is C1-8 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, pyranyl, thiopyranyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, or amino wherein R₁ is optionally substituted by one or more R_b;

25

30 R_b is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkoxy, aryloxy, C1-8 alkoxy carbonyl, aryloxycarbonyl, C1-8 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkanoylamino, aroylamino, C1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be

independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxyazinyl, alkoxy carbonylamino, aryloxy carbonylamino, C1-8 alkyl carbamoyloxy, aryl carbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxyazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R_b may be further optionally substituted by one or more R_c;

R_c is selected from the group consisting of C1-8 alkyl, C3-6 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxyazinyl, C1-8 alkoxy, aryloxy, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

35 R₃ is H, C1-8 alkyl, C3-7 cycloalkyl or aryl wherein R₃ is optionally substituted by one or more R_d;

40 R_d is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxyazinyl, C1-8 alkoxy, aryloxy, alkanoyl, aroyl, C1-8 alkoxy carbonyl,

aryloxycarbonyl, C1-8 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoazinyl, C1-8 alkanoylamino, aroylamino, C1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, 10 piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and quinoazinyl, C1-8 alkylcarbamoylamino, C1-8 alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, 15 piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl, 20 quinoazinyl, carbazolyl, phenothiazinyl and phenoazinyl, alkoxy carbonylamino, aryloxycarbonylamino, C1-8 alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, 25 piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl, 30 and phenoazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R_d may be further optionally substituted by one or more R_e;

R_e is selected from the group consisting of C1-8 alkyl, C3-6 cycloalkyl, aryl, arylalkyl, C1-8 alkoxy, aryloxy, arylalkoxy, aroyl, amino, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

R_s is H or alkyl;
40 R₆ is H, C1-8 alkyl, C3-7 cycloalkyl or aryl wherein R₆ is optionally substituted by one or more R_f;

45 R_f is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl,

5 morpholiny, thiomorpholiny, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkoxy, aryloxy, arylC1-8alkoxy, heteroarylC1-8alkoxy, C1-8 alkoxy carbonyl, aryloxy carbonyl, C1-8 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholiny, thiomorpholiny, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkanoylamino, aroylamino, C1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylC1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholiny, thiomorpholiny, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, alkoxy carbonylamino, aryloxy carbonylamino, C1-8 alkyl carbamoyloxy, aryl carbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholiny, thiomorpholiny, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R_f may be further optionally substituted by one or more R_g;

40

45 R_g is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl optionally substituted by halogen, C1-3alkyl or C1-3alkoxy; heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholiny, thiomorpholiny, piperazinyl and indolinyl;

heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl,
oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl,
triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl,
pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl,
benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl,
quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoazinyl,
C1-8 alkoxy, aryloxy, arylC1-8alkoxy, C1-8 alkoxy carbonyl,
aryloxycarbonyl, C1-8 alkanoyloxy, aroyloxy, carbamoyl wherein the
nitrogen atom may be independently mono or di-substituted by C1-8 alkyl,
aryl, heterocyclyl selected from the group consisting of pyrrolidinyl,
piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or
heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl,
oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl,
triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl,
pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl,
benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl,
quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoazinyl,
C1-8 alkanoylamino, aroylamino, C1-8 alkylthio wherein the sulfur atom
may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom
may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen
atom may be independently substituted by alkyl, aryl, heterocyclyl
selected from the group consisting of pyrrolidinyl, piperidinyl,
morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl
selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,
thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl,
tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl,
indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl,
benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl,
quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl or phenoazinyl,
alkoxy carbonylamino, aryloxycarbonylamino, C1-8 alkyl carbamoyloxy,
aryl carbamoyloxy, alkylsulfonylamino, arylsulfonylamino,
alkylaminosulfonyl and arylaminosulfonyl, amino wherein the nitrogen
atom may be independently mono or di-substituted by alkyl, aryl,
heterocyclyl selected from the group consisting of pyrrolidinyl,
piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or
heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl,
oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl,
triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl,
pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl,
benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl,
quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoazinyl,
halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

- R_h is selected from the group consisting of C1-8 alkyl, aryl, C1-8 alkoxy carbonyl, aryloxycarbonyl, arylC1-8alkoxycarbonyl, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with a group selected from C1-8 alkyl, C3-7 cycloalkyl, aryl, arylC1-8alkyl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoaxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoaxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, halogen, hydroxy, carboxy and cyano;
- 15 R_g is a heteroaryl ring selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoaxazolyl, isothiazolyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, indolizinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, indazolyl, benzimidazolyl, benzthiazolyl, benzoaxazolyl, triazolyl, tetrazolyl, purinyl, quinolizinyl, quinolinyl, isoquinolinyl, cinnolinyl, phthalazinyl, quinazolinyl, quinoxalinyl, naphthyridinyl, pteridinyl, carbazolyl, acridinyl and phenazinyl, wherein any of the above R_g can be optionally substituted by one or more R_j;
- 20 R_j is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoaxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, arylalkyl, alkoxy, aryloxy, arylalkoxy, alkoxy carbonyl, aryloxycarbonyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoaxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylalkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl

selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,
 thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl,
 thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl,
 benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl,
 quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl
 and phenoxazinyl, alkoxycarbonylamino, aryloxycarbonylamino, C1-8
 alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino,
 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be
 independently mono or di-substituted by alkyl, aryl, heterocycl selected from
 the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl,
 piperazinyl and indolinyl, or heteroaryl selected from the group consisting of
 furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl,
 oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl,
 pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl,
 benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl,
 quinoxaliny, carbazolyl, phenothiazinyl and phenoxazinyl, halogen, hydroxy,
 oxo, carboxy, cyano, nitro, amidino and guanidino, R_j may be further optionally
 substituted by one or more R_k;

 20 R_k is selected from the group consisting of alkyl, cycloalkyl, aryl,
 heterocycl selected from the group consisting of pyrrolidinyl,
 piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl;
 heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl,
 oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl,
 triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl,
 pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl,
 benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl,
 quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoxazinyl,
 alkoxy, aryloxy, arylalkoxy, alkoxycarbonyl, aryloxycarbonyl,
 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be
 independently mono or di-substituted by alkyl, aryl, heterocycl selected
 from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl,
 thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the
 group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl,
 imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl,
 thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl,
 isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl,
 benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl,
 quinoxaliny, carbazolyl, phenothiazinyl and phenoxazinyl,
 alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be
 oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be
 oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom
 may be independently substituted by alkyl, aryl, heterocycl selected
 from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl,
 thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the
 group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl,

imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl,
 thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl,
 isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl,
 5 benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl,
 quinoxalinyl, carbazolyl, phenothiazinyl and phenoazinyl,
 alkoxycarbonylamino, aryloxycarbonylamino, arylalkoxycarbonylamino,
 10 arylalkoxycarbonylaminoalkyl, C1-8 alkylcarbamoyloxy,
 arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino,
 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom
 15 may be independently mono or di-substituted by alkyl, aryl, heterocyclyl
 selected from the group consisting of pyrrolidinyl, piperidinyl,
 morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl
 selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,
 thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl,
 20 tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl,
 indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl,
 benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl,
 quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoazinyl,
 halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

20 X is O or S.

More preferred compounds of the formula (I) are those wherein:

25 Y is O or S;

R₁ is C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group
 30 consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, pyranlyl,
 thiopyranyl, piperazinyl and indolinyl, heteroaryl selected from the group consisting of
 furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl,
 35 pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl,
 benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl or
 amino wherein R1 is optionally substituted by one or more R_b;

R_b is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, phenyl,
 naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl,
 40 piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, heteroaryl
 selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,
 thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl,
 indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl,
 45 quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxy, aryloxy,
 C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl
 wherein the nitrogen atom may be independently mono or di-substituted by C1-8
 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl,

piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of

5 pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl . or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5

10 alkoxy carbonylamino, aryloxy carbonylamino, C1-5 alkyl carbamoyloxy, aryl carbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl,

15 piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R_b may be further optionally substituted by one or more

20 R_c;

R_c is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl, aryl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl and pyridinyl, C1-5 alkoxy, aryloxy, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

25

30

35 R₂ is H or C1-3 alkyl;

R₃ is H, C1-5 alkyl, C3-7 cycloalkyl or aryl, wherein R₃ is optionally substituted by one or more R_d;

40 R_d is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxy, aryloxy, C1-5 alkanoyl,

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5 aroyl, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thieryl, 10 pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, 15 thieryl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, 20 arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thieryl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, 25 pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R_d may be further optionally substituted by one or more R_e;

30 35 R_e is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl, aryl, arylalkyl, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, aroyl, amino, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

40 45 R₄ is H or C1-3 alkyl;

R₅ is H or C1-8 alkyl;

R₆ is H, C1-5 alkyl, C3-7 cycloalkyl or aryl wherein R₆ is optionally substituted by one or more R_f;

R_f is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, heteroarylC1-5alkoxy, C1-5 alkoxy carbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylC1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny, C1-5 alkoxy carbonylamino, aryloxycarbonylamino, C1-5 alkyl carbamoyloxy, aryl carbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R_f may be further optionally substituted by one or more R_g;

R_g is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, aryl optionally substituted by halogen, methyl or methoxy; heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny,

benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, C1-5
5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkanoylamino, aroylamino, C1-5
10 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5
15 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl,
20 pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;
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R₄ is selected from the group consisting of C1-5 alkyl, aryl, C1-5 alkoxycarbonyl, aryloxycarbonyl, arylC1-5alkoxy carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with a group selected from C1-5 alkyl, C3-7 cycloalkyl, aryl, arylC1-5alkyl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, halogen, hydroxy, carboxy and cyano;

R_j is alkoxy, aryloxy or hydroxy;

- 5 R₈ is a heteroaryl ring selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, indolizinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, indazolyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolizinyl, quinolinyl, isoquinolinyl, cinnolinyl, phthalazinyl, quinazolinyl, quinoxalinyl, naphthyridinyl, pteridinyl, carbazolyl, acridinyl and phenazinyl, wherein any of the above R₈ can be optionally substituted by one or more R_j;
- 10 R_j is selected from the group consisting of C1-8alkyl, C3-7cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl; arylC1-8alkyl, C1-8alkoxy, aryloxy, arylC1-8alkoxy, C1-8alkoxycarbonyl, aryloxycarbonyl, C1-8alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8alkanoylamino, aroylamino, C1-8alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylC1-8alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group

consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoxazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R_j may be further optionally substituted by one or more R_k;

R_k is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkoxy, aryloxy, arylC1-8alkoxy, C1-8alkoxycarbonyl, aryloxycarbonyl, C1-8alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoxazinyl, alkanoylamino, aroylamino, C1-8alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-8alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8alkoxycarbonylamino, aryloxycarbonylamino, arylC1-8alkoxycarbonylamino, arylalkoxycarbonylaminoC1-8alkyl, C1-8alkylcarbamoyloxy, arylcarbamoyloxy, C1-8alkylsulfonylamino, arylsulfonylamino, C1-8alkylaminosulfonyl, arylaminosulfonyl, amino

wherein the nitrogen atom may be independently mono or di-substituted by C1-8alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, 5 thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, 10 isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino.

15 Even more preferred compounds of the formula (I) are those wherein:

Y is O;

20 R₁ is C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, pyranyl and thiopyranyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, or amino 25 wherein R₁ is optionally substituted by one or more R_b;

25 R_b is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, 30 thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl; C1-5 alkoxy, aryloxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the 35 group consisting of pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio 40 wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl or aryl; C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 45 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from

the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy, cyano and nitro, R_b may be further optionally substituted by one or more R_c;

R_c is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl, aryl, C1-5 alkoxy, aryloxy, halogen, hydroxy, oxo, carboxy, and cyano;

R₂ is H or methyl;

R₃ is H, C1-5 alkyl, C3-7 cycloalkyl or phenyl, wherein R₃ is optionally substituted by one or more R_d;

R_d is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5 alkoxy, aryloxy, aroyl, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy and cyano, R_d may be further optionally substituted by one or more R_e;

R_e is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl, aryl, arylC1-5alkyl, C1-5 alkoxy, aryloxy, arylC1-3alkoxy, aroyl, amino, halogen, hydroxy, oxo, carboxy and cyano;

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R₄ is H or methyl;

10 R₅ is H or C1-5 alkyl;

R₆ is H, C1-5 alkyl, C3-7 cycloalkyl, phenyl or naphthyl wherein R₆ is optionally substituted by one or more R_f;

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R_f is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, pyridylC1-5alkoxy, thienylC1-5alkoxy, furanylC1-5alkoxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylC1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl,

quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy and cyano, R_f may be further optionally substituted by one or more R_g;

R_g is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl,
 5 phenyl optionally substituted by halogen, methyl or methoxy; naphthyl
 optionally substituted by halogen, methyl or methoxy; heterocyclyl
 selected from the group consisting of pyrrolidinyl, piperidinyl,
 morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl
 10 selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,
 thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl,
 pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl,
 benzthiazolyl, benzoaxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and
 quinoxalinyl, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, C1-5
 15 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl
 wherein the nitrogen atom may be independently mono or di-substituted
 by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of
 piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the
 group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl,
 20 imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl,
 benzimidazolyl, benzthiazolyl, benzoaxazolyl, quinolinyl and isoquinolinyl,
 C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom
 may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom
 25 may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen
 atom may be independently substituted by C1-5 alkyl, aryl, heterocyclyl
 selected from the group consisting of piperidinyl, morpholinyl and
 piperazinyl or heteroaryl selected from the group consisting of furanyl,
 thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl,
 30 benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoaxazolyl,
 quinolinyl, isoquinolinyl, C1-5 alkoxycarbonylamino,
 aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5
 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl,
 arylaminosulfonyl, amino wherein the nitrogen atom may be
 35 independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl
 selected from the group consisting of pyrrolidinyl, piperidinyl,
 morpholinyl and piperazinyl or heteroaryl selected from the group
 consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl,
 pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl,
 benzthiazolyl, benzoaxazolyl, quinolinyl and isoquinolinyl, halogen,
 hydroxy, oxo, carboxy and cyano;
 40

R_h is selected from the group consisting of C1-5 alkyl, phenyl, naphthyl, C1-5
 45 alkoxycarbonyl, aryloxycarbonyl, arylC1-3alkoxycarbonyl, carbamoyl wherein
 the nitrogen atom may be optionally mono or di-substituted with a group selected
 from C1-5 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, arylC1-3alkyl, heterocyclyl

selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, carboxy and cyano;

5 Z is O or S;

10

R₈ is a heteroaryl ring selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, indolizinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, indazolyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, 15 quinolizinyl, quinolinyl, isoquinolinyl, cinnolinyl, phthalazinyl, quinazolinyl, quinoxalinyl, naphthyridinyl, pteridinyl, carbazolyl, acridinyl and phenazinyl, wherein any of the above R₈ can be optionally substituted by one or more groups of the formula R_j;

20

R_j is selected from the group consisting of C1-5alkyl, C3-6cycloalkyl, phenyl, naphthyl, heterocyclcyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, 25 quinolinyl and isoquinolinyl, arylC1-5alkyl, C1-5alkoxy, aryloxy, arylC1-5alkoxy, C1-5alkoxycarbonyl, aryloxycarbonyl, C1-5alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5alkyl, aryl, heterocyclcyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group 30 consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5alkanoylamino, aroylamino, C1-5alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, 35 arylC1-5alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, heterocyclcyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, 40 indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5alkylsulfonylamino, arylsulfonylamino, C1-5alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, 45 aryl, heterocyclcyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl,

thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R_j may be further optionally substituted by one or more R_k;

5 R_k is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, tetrazolyl and pyridinyl, C1-3 alkoxy, aryloxy, arylC1-3alkoxy, C1-3alkoxycarbonyl, aryloxycarbonyl, C1-3alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, aryl, heterocyclyl selected from the group consisting of morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, and pyridinyl, C1-3alkanoylamino, aroylamino, C1-3alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-3alkyl, phenyl, naphthyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl and pyridinyl, C1-3alkoxycarbonylamino, aryloxycarbonylamino, arylC1-3alkoxycarbonylamino, benzyloxycarbonylaminoC1-5alkyl, C1-3alkylcarbamoyloxy, arylcarbamoyloxy, C1-3alkylsulfonylamino, arylsulfonylamino, C1-3alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3alkyl, aryl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolylpyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy, cyano and nitro;

20 35 and

X is O.

25 40 Yet even more preferred compounds of the formula (I) are those wherein:

45 R₁ is C1-5 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl, piperazinyl, pyranyl and thiopyranyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl,

imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, or amino, wherein R₁ is optionally substituted by one or more R_b;

- 5 R_b is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-3 alkoxy, phenoxy, C1-3 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5alkyl, phenyl or naphthyl; C1-5 alkoxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy and cyano, R_b may be further optionally substituted by one or more R_c;
- 30 R_c is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, aryl, C1-3 alkoxy, phenoxy, halogen, hydroxy, oxo, carboxy and cyano;

R₂ is H;

- 35 R₃ is C1-5 alkyl, C3-6 cycloalkyl or phenyl, wherein R₃ is optionally substituted by one or more R_d;
- 40 R_d is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, quinolinyl andisoquinolinyl, C1-5 alkoxy, phenoxy, aroyl, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl,
- 45

5 morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, C1-5 alkanoylamino, aroylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, phenylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-3 alkyl, phenyl or heteroaryl selected the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, C1-5 alkoxy carbonylamino, C1-5 alkyl carbamoyloxy,
10 aryl carbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, phenyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, halogen, hydroxy, oxo, carboxy and cyano, R_d may be further optionally substituted by one or more R_e;

15 R_e is selected from the group consisting of C1-5 alkyl, C5-6 cycloalkyl, phenyl, naphthyl, arylC1-3alkyl, C1-5 alkoxy, phenoxy, arylC1-3alkoxy, aroyl, amino, halogen, hydroxy, oxo, carboxy and cyano;
20

25 wherein the configuration at the stereocenter defined by R₂ and R₃ and the carbon they are attached to is L;

30 R₄ is H;

35 R₅ is H or C1-3 alkyl;

40 R₆ is H, C1-5 alkyl, C3-6 cycloalkyl or phenyl. wherein R₆ is optionally substituted by one or more R_f;

45 R_f is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5 alkoxy, aryloxy, arylC1-3alkoxy, pyridylC1-5alkoxy, thienylC1-5alkoxy, furanylC1-5alkoxy, C1-5 alkoxy carbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, C1-5 alkanoylamino, aroylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a

5 sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylC1-3alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl or phenyl; C1-5 alkoxy carbonylamino, C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, halogen, hydroxy, 10 oxo, carboxy and cyano, Rf may be further optionally substituted by one or more Rg;

15 Rg is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl optionally substituted by halogen, methyl or methoxy; heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, pyrimidinyl, pyrazinyl and indolyl, C1-5 alkoxy, aryloxy, arylC1-3alkoxy, C1-5 alkoxy carbonyl, aryloxycarbonyl, C1-5 20 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or aryl; C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl or aryl; C1-5 25 alkoxy carbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or aryl; 30 halogen, hydroxy, oxo, carboxy and cyano;

35 Rh is selected from the group consisting of C1-5 alkyl, phenyl, C1-5 alkoxy carbonyl, aryloxycarbonyl, arylC1-3alkoxycarbonyl, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with C1-5 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, arylC1-3alkyl, halogen, hydroxy, carboxy and cyano;

40 wherein Z is O;

45 Rg is a heteroaryl ring selected from the group consisting of oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl,

benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, wherein any of the above R₈ can be optionally substituted by one or more R_j;

R_j is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl, naphthyl, morpholinyl, piperazinyl, furanyl, thienyl, pyrrolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, arylC1-3alkyl, C1-3alkoxy, aryloxy, arylC1-3alkoxy, C1-3alkoxycarbonyl, aryloxycarbonyl, C1-3alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3alkyl, phenyl, naphthyl, piperidinyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl or isoquinolinyl; C1-3alkanoylamino, aroylamino, C1-3alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylC1-3alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-3 alkyl, phenyl, naphthyl, piperidinyl, morpholinyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl or isoquinolinyl; C1-3alkoxycarbonylamino, aryloxycarbonylamino, C1-3 alkylcarbamoyloxy, arylcarbamoyloxy, C1-3alkylsulfonylamino, arylsulfonylamino, C1-3alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, phenyl, naphthyl, piperidinyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl or isoquinolinyl; halogen, hydroxy, oxo, carboxy, cyano and nitro, R_j may be further optionally substituted by one or more R_k;

R_k is selected from the group consisting of methyl, C5-6 cycloalkyl, phenyl, morpholinyl, furanyl, thienyl, pyrrolyl, tetrazolyl, pyridinyl, methoxy, phenoxy, benzyloxy, methoxycarbonyl, acetyloxy, benzoxyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, phenyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl or pyridinyl; acetylarnino, benzoylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by methyl, phenyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl or pyridinyl; arylC1-3alkoxycarbonylamino, benzylloxycarbonylaminoC1-3alkyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3alkyl, phenyl, naphthyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl or isoquinolinyl, halogen, hydroxy, oxo, carboxy, cyano and nitro.

45

Still yet even more preferred compounds of the formula (I) are those wherein:

- 5 R₁ is C1-3 alkyl, C5-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl, piperazinyl, pyranyl and thiopyranyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, or amino, wherein R₁ is optionally substituted by one or more R_b;
- 10 R_b is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-3 alkoxy, C1-3 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, phenyl or heteroaryl selected from the group consisting of pyrrolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl and benzthiazolyl; C1-5 alkanoylamino, aroylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-3 alkyl or phenyl; C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, phenyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of pyrrolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl; halogen, hydroxy, oxo, carboxy and cyano, R_b may be further optionally substituted by one or more R_c;
- 15 30 R_c is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, C1-3 alkoxy, halogen and hydroxy;
- 35 R₃ is C1-5 alkyl, C5-6 cycloalkyl or phenyl wherein R₃ is optionally substituted by one or more R_d;
- 40 R_d is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, 4-piperidinyl, 4-morpholinyl, piperazinyl, furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-5 alkoxy, phenoxy, aroyl, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or phenyl; C1-5 alkanoylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-3 alkyl or phenyl; C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be

independently mono or di-substituted by C1-3 alkyl or phenyl; halogen, hydroxy, oxo, carboxy and cyano, R_d may be further optionally substituted by one or more R_e;

5 R_e is selected from the group consisting of C1-5 alkyl, C5-6 cycloalkyl, phenyl, benzyl, C1-5 alkoxy, phenoxy, benzyloxy, aroyl, halogen, hydroxy, oxo, carboxy and cyano;

10 R₆ is H, C1-5 alkyl or phenyl wherein R₆ is optionally substituted by one or more R_f,

R_f is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-3 alkoxy, benzyloxy, pyridyl, C1-3alkoxy, thienylC1-3alkoxy, furanylC1-3alkoxy, C1-3 alkoxycarbonyl, phenoxyoxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; C1-5 alkanoylamino, aroylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl or phenyl; C1-3 alkoxycarbonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or phenyl; halogen, hydroxy, oxo, carboxy and cyano, R_f may be further optionally substituted by one or more R_g;

25 R_g is selected from the group consisting of C1-3 alkyl, phenyl optionally substituted by halogen, methyl or methoxy; heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl and pyridinyl, C1-3 alkoxy, aryloxy, benzyloxy, C1-5 alkoxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or phenyl; C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl or phenyl; C1-5 alkoxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-3 alkylsulfonylamino, arylsulfonylamino, C1-3 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; halogen, hydroxy, oxo, carboxy and cyano;

40

45 R_h is selected from the group consisting of C1-3 alkyl, phenyl, C1-3 alkoxycarbonyl, phenoxyoxycarbonyl, benzyloxy, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with C1-5 alkyl, phenyl, benzyl, halogen, hydroxy, carboxy and cyano;

5 R₈ is a heteroaryl ring selected from the group consisting of oxazolyl, thiazolyl, imidazolyl, pyridyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, wherein any of the above R₈ can be optionally substituted by one or more R_j;

10 R_j is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl, naphthyl, morpholinyl, piperazinyl, furanyl, thienyl, pyrrolyl, tetrazolyl, pyridinyl, benzyl, C1-3alkoxy, phenoxy, benzyloxy, C1-3alkoxycarbonyl, acetyloxy, benzoyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by methyl, phenyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl or pyridinyl; acetyl amino, benzoyl amino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by methyl, phenyl, thiazolyl, imidazolyl or pyridinyl; C1-3 alkoxy carbonyl amino, C1-3 alkyl carbamoyloxy, aryl carbamoyloxy, C1-3alkylsulfonyl amino, arylsulfonyl amino, amino wherein the nitrogen atom may be independently mono or di-substituted by methyl, phenyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl or pyridinyl; halogen, hydroxy, carboxy, cyano and nitro, R_j may be further optionally substituted by one or more R_k;

25 R_k is selected from the group consisting of methyl, C5-6 cycloalkyl, phenyl, furanyl, thienyl, pyrrolyl, pyridinyl, methoxy, phenoxy, benzyloxy, methoxycarbonyl, acetyloxy, benzoyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by methyl, phenyl, furanyl or thienyl; acetyl amino, benzoyl amino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by methyl, phenyl, furanyl, thienyl, pyrrolyl, oxazolyl and thiazolyl, benzyl oxy carbonyl amino, benzyl oxy carbonyl amino C1-5alkyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3alkyl, phenyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl and pyridinyl, halogen, hydroxy, carboxy, cyano and nitro.

40 Even much more preferred compounds of the formula (I) are those wherein:

45 R₁ is C5-6 cycloalkyl, phenyl, naphthyl, piperidinyl, morpholinyl, piperazinyl, furanyl, thienyl, pyrrolyl, pyranyl, thiopyranyl or amino wherein R₁ is optionally substituted by one or more R_b;

- 5 R_b is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl, furanyl, thienyl, pyrrolyl, imidazolyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, C1-3 alkoxy, C1-3 alkoxycarbonyl, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; C1-5 alkanoylamino, aroylamino, ureido wherein either nitrogen atom may be independently substituted by C1-3alkyl or phenyl; C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3alkyl or phenyl;, halogen, hydroxy, oxo, carboxy and cyano, R_b may be further optionally substituted by one or more R_c;
- 10 R_c is selected from the group consisting of C1-3 alkyl, C1-3 alkoxy, halogen and hydroxy;
- 15 R_d is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, 4-piperidinyl, furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-3alkoxy, C1-5alkoxycarbonyl, C1-5alkanoyloxy, benzyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3alkyl or phenyl; C1-5alkanoylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, C1-3alkoxycarbonylamino, C1-3alkylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, halogen, hydroxy, oxo, carboxy and cyano, R_d may be further optionally substituted by one or more R_e;
- 20 R_e is selected from the group consisting of C1-3 alkyl, phenyl, benzyl, C1-3 alkoxy, phenoxy, benzyloxy, benzoyl, halogen, hydroxy, oxo, carboxy and cyano;
- 25 R_f is H or methyl;
- 30 R₆ is C1-5 alkyl or phenyl, wherein R₆ is optionally substituted by one or more groups of the formula R_f,
- 35 R_f is selected from the group consisting of methyl, C3-6 cycloalkyl, phenyl, naphthyl, furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-3 alkoxy, benzyloxy, C1-5 alkanoylamino, aroylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, C1-3 alkoxycarbonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or phenyl; halogen, hydroxy, oxo, carboxy and cyano, R_f may be further optionally substituted by one or more R_g;
- 40 R_g is selected from the group consisting of C1-3 alkyl, phenyl optionally substituted by halogen or methyl; C1-3 alkoxy, aryloxy, benzyloxy, C1-3

5

alkoxycarbonyl, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; C1-5 alkanoylamino, aroylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; halogen, hydroxy, oxo, carboxy and cyano;

10

R_h is selected from the group consisting of C1-3 alkyl, phenyl, C1-3 alkoxy, carbonyl, benzyloxy and carboxy;

15

R_g is a heteroaryl ring selected from the group consisting of oxazolyl, thiazolyl, imidazolyl, pyridyl, benzimidazolyl, benzthiazolyl and benzoxazolyl, wherein any of the above R_g can be optionally substituted by one or more R_j;

20

R_j is selected from the group consisting of methyl, cyclohexyl, phenyl, furanyl, thienyl, benzyl, methoxy, phenoxy, benzyloxy, methoxycarbonyl, acetyloxy, benzoyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by methyl, phenyl, furanyl or thienyl; acetylarnino, benzoylamino, ureido wherein either nitrogen atom may be independently substituted by methyl or phenyl; methoxycarbonylarnino, C1-3 alkylsulfonylarnino, arylsulfonylarnino, amino wherein the nitrogen atom may be independently mono or di-substituted by methyl, phenyl, furanyl or thienyl; halogen, hydroxy, carboxy and cyano, R_j may be further optionally substituted by one or more R_k;

25

R_k is selected from the group consisting of methyl, phenyl, furanyl, thienyl, methoxy, phenoxy, benzyloxy, methoxycarbonyl, acetyloxy, benzoyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by methyl or phenyl; acetylarnino, benzoylamino, ureido wherein either nitrogen atom may be independently substituted by methyl or phenyl; benzyloxycarbonylarnino, benzyloxycarbonylarninoC1-3alkyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3alkyl, phenyl, furanyl or thienyl; halogen, hydroxy, carboxy, cyano and nitro.

30

Yet even more preferred compounds of the formula (I) are those wherein:

A is -C(O)- or -SO₂-;

40

R₁ is cyclohexyl, phenyl, naphthyl, piperidinyl, morpholinyl, piperazinyl, pyranyl, thiopyranyl or amino, wherein R₁ is optionally substituted by one or more R_b;

45

R_b is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl, furanyl, thienyl, pyrrolyl, imidazolyl, indolyl, benzofuranyl, benzothienyl,

benzimidazolyl, benzthiazolyl, benzoxazolyl, C1-3 alkoxy, C1-3 alkoxycarbonyl, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; C1-5 alkanoylamino, aroylamino, C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl; halogen, hydroxy, oxo, carboxy and cyano, R_b may be further optionally substituted by one or more R_c;

R_c is selected from the group consisting of C1-3 alkoxy, halogen and hydroxy;

10 R₃ is C1-5 alkyl or C5-6 cycloalkyl, wherein R₃ is optionally substituted by one or more R_d;

15 R_d is selected from the group consisting of methyl, C3-6 cycloalkyl, phenyl, thienyl, imidazolyl, pyridinyl, indolyl, C1-4 alkoxy, C1-5 alkanoylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, halogen, hydroxy, oxo, carboxy and cyano, R_d may be further optionally substituted by one or more R_e;

20 R_e is selected from the group consisting of methyl, phenyl, benzyl, methoxy, phenoxy, benzyloxy, benzoyl, halogen and hydroxy;

25

30 R_f is selected from the group consisting of C3-6 cycloalkyl, phenyl, naphthyl, thienyl, imidazolyl, pyridinyl, indolyl, methoxy, benzyloxy, C1-3 alkanoylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, methoxycarbonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl; halogen, hydroxy, carboxy and cyano, R_f may be further optionally substituted by one or more R_g;

35 R_g is selected from the group consisting of methyl, phenyl optionally substituted by halogen or methyl; methoxy, phenoxy, benzyloxy, methoxycarbonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; halogen, hydroxy and carboxy;

45

R_g is a heteroaryl ring selected from the group consisting of oxazolyl, thiazolyl, imidazolyl, pyridyl, benzthiazolyl and benzoxazolyl, wherein any of the above R_g can be optionally substituted by one or more R_j;

5 R_j is selected from the group consisting of methyl, phenyl, furanyl, thienyl, benzyl, methoxy, methoxycarbonyl, acetyloxy, benzoyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by methyl or phenyl; acetyl amino, benzoyl amino, ureido wherein either nitrogen atom may be independently substituted by methyl or phenyl; methoxycarbonyl amino, amino wherein the nitrogen atom may be independently mono or di-substituted by methyl or phenyl; halogen, hydroxy, carboxy and cyano, R_j may be further optionally substituted by one or more R_k;

10 15 R_k is selected from the group consisting of methyl, phenyl, methoxy, phenoxy, benzyloxy, methoxycarbonyl, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by methyl or phenyl; ureido wherein either nitrogen atom may be independently substituted by methyl or phenyl; benzyloxycarbonyl amino, benzyloxycarbonyl amino C1-5alkyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3alkyl, phenyl, furanyl or thienyl; halogen, hydroxy, carboxy, cyano and nitro.

20 25 Penultimately preferred compounds of the formula (I) are those wherein:

R₁ is cyclohexyl, phenyl, naphthyl, piperidinyl, morpholinyl, piperazinyl, pyranyl or thiopyranyl, wherein R₁ is optionally substituted by one or more R_b;

30 R_b is selected from the group consisting of, pyrrolyl, imidazolyl, indolyl, benzimidazolyl, methoxy, methoxycarbonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl; halogen, hydroxy and carboxy, R_b may be further optionally substituted by one or more R_c;

35 R_c is selected from the group consisting of methoxy, halogen and hydroxy;

40 45 R_d is selected from the group consisting of methyl, C3-6 cycloalkyl, phenyl, C1-4 alkoxy, C1-3 alkanoyl amino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, halogen, hydroxy, oxo, carboxy and cyano, R_d may be further optionally substituted by one or more R_e;

R_e is selected from the group consisting of methyl, phenyl, methoxy, halogen and hydroxy;

R₅ is H;

5 R_f is selected from the group consisting of C5-6 cycloalkyl, phenyl, naphthyl, thienyl, indolyl, methoxy, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, methoxycarbonylamino, halogen, hydroxy, carboxy and cyano, R_f may be further optionally substituted by one or more R_g;

10 R_g is selected from the group consisting of methyl, phenyl optionally substituted by halogen; methoxy, phenoxy, benzyloxy, methoxycarbonyl, halogen, hydroxy and carboxy;

15 R₈ is a heteroaryl ring selected from the group consisting of oxazolyl, pyridyl, benzthiazolyl and benzoxazolyl, wherein any of the above R₈ can be optionally substituted by one or more R_j;

20 R_j is selected from the group consisting of methyl, phenyl, benzyl, methoxy, methoxycarbonyl, acetyloxy, benzyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by methyl or phenyl; methoxycarbonylamino, halogen, hydroxy and carboxy, R_j may be further optionally substituted by one or more R_k;

25 R_k is selected from the group consisting of methyl, phenyl, methoxy, methoxycarbonyl, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by methyl or phenyl; benzyloxycarbonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by methyl or phenyl; halogen, hydroxy and carboxy.

30

Ultimately preferred compounds of the formula(I) are those wherein:

35

R₁ is phenyl or 4-morpholinyl, wherein R₁ is optionally substituted by one or more R_b;

40 R_b is selected from the group consisting of benzimidazolyl, methoxy and dimethylamino, R_b may be further optionally substituted by a halogen atom;

R₃ is C1-5 alkyl wherein R₃ is optionally substituted by one or more R_d;

45 R_d is selected from the group consisting of C3-6 cycloalkyl and phenyl, R_d may be further optionally substituted by one or more R_e;

R_e is selected from the group consisting of methyl and halogen;

5 R₆ is C1-5 alkyl optionally substituted by one or more R_f;

R_f is selected from the group consisting of C5-6 cycloalkyl, phenyl, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, and halogen, R_f may be further optionally substituted by one or more R_g;

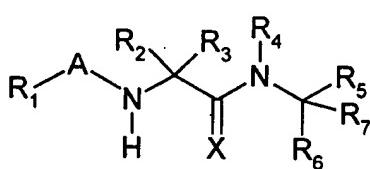
10 R_g is selected from the group consisting of methyl, methoxy, methoxycarbonyl, halogen and hydroxy;

15 R₈ is a heteroaryl ring selected from the group consisting of oxazolyl, pyridyl, benzthiazolyl and benzoxazolyl, wherein any of the above R₈ can be optionally substituted by one or more R_j;

20 R_j is selected from the group consisting of phenyl, methoxycarbonyl, carbamoyl wherein the nitrogen atom may be independently mono or disubstituted by methyl or phenyl; methoxycarbonylamino and halogen, R_j may be further optionally substituted by one or more R_k;

R_k is selected from the group consisting of phenyl, methoxycarbonyl, carbamoyl, benzyloxycarbonylamino and halogen.

25 In another embodiment of the invention there are provided novel compounds of the formula (Ia):



30 (Ia)

wherein:

35 A is -C(Y)- or -SO₂-

Y is O, S or NR_a wherein R_a is selected from the group consisting of H, alkyl, aryl, alkoxy, aryloxy, alkylamino and arylamino;

40

R₁ is alkyl, cycloalkyl, aryl, heterocycl, heteroaryl or amino wherein R₁ is optionally substituted by one or more R_b;

5 R_b is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocycl, heteroaryl, alkoxy, aryloxy, alkoxycarbonyl, aryloxycarbonyl, alkanoyl, aroyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocycl or heteroaryl, alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocycl or heteroaryl, alkoxycarbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocycl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R_b may be further optionally substituted by one or more R_c;

20 R_c is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocycle, heteroaryl, arylalkyl, alkoxy, aryloxy, arylalkoxy, alkanoyl, aroyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocycl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

25 R₂ is H or alkyl;

R₃ is H, alkyl, cycloalkyl, aryl, heterocycl or heteroaryl, wherein R₃ is optionally substituted by one or more groups of the formula R_d;

30 R_d is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocycl, heteroaryl, alkoxy, aryloxy, arylalkoxy, alkoxycarbonyl, aryloxycarbonyl, alkanoyl, aroyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocycl or heteroaryl, alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocycl or heteroaryl, alkoxycarbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocycl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R_d may be further optionally substituted by one or more R_e;

R_c is selected from the group consisting of alkyl, cycloalkyl, aryl, arylalkyl, alkoxy, aryloxy, arylalkoxy, alkanoyl, aroyl, amino, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

5

R₄ is H or alkyl;

10

R₅ is H, alkyl or cycloalkyl;

15

R₆ is H, alkyl, cycloalkyl, aryl, heterocyclyl or heteroaryl, wherein R₆ is optionally substituted by one or more groups of the formula R_f;

20

R_f is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkoxy, aryloxy, alkanoyl, aroyl, arylalkoxy, heteroarylalkoxy, alkoxycarbonyl, aryloxycarbonyl, alkanoyloxy, aryloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylalkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkoxycarbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R_f may be further optionally substituted by one or more R_g;

25

R_g is selected from the group consisting of alkyl, cycloalkyl, aryl optionally substituted by halogen, C1-5alkyl or C1-5alkoxy, heterocyclyl, heteroaryl, alkoxy, aryloxy, arylalkoxy, alkoxycarbonyl, aryloxycarbonyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl; alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl; alkoxycarbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl; halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

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45

or R₅ together with R₆ form a 3 to 6 membered carbocyclic ring, the carbocyclic ring being optionally substituted with one or more R_h;

5 R_h is selected from the group consisting of alkyl, aryl, alkoxycarbonyl, aryloxycarbonyl, arylalkoxycarbonyl, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with a group selected from alkyl, cycloalkyl, aryl, arylalkyl, heterocyclyl or heteroaryl; halogen, hydroxy, carboxy and cyano;

10 R₇ is R₈-C(Z)-;

15 wherein Z is O, S, or NR_i wherein R_i is selected from the group consisting of H, alkyl, aryl, alkoxy, aryloxy and hydroxy;

20 R₈ is a 5-8 membered monocyclic heteroaryl or 8-11 membered bicyclic heteroaryl ring system, each of the monocyclic or bicyclic ring systems having 1-4 of the same or different heteroatoms selected from the group consisting of N, O and S wherein any of the above R₈ can be optionally substituted by one or more R_j;

25 R_j is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, arylalkyl, alkoxy, aryloxy, alkanoyl, aroyl, arylalkoxy, alkoxycarbonyl, aryloxycarbonyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylalkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl; alkoxycarbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl; halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R_j may be further optionally substituted by one or more R_k;

35 R_k is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkoxy, aryloxy, arylalkoxy, alkoxycarbonyl, aryloxycarbonyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkoxycarbonylamino, aryloxycarbonylamino, arylalkoxycarbonylamino, arylalkoxycarbonylaminoalkyl, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein

the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, wherein R_k may be further optionally substituted by R_l;

5

R_l is selected from the group consisting of alkyl, cycloalkyl, aryl, and benzyl;

X is O, S or N-OH;

10

and the pharmaceutically acceptable derivatives thereof;

with the following provisos:

- 15 when R₆ is alkyl the alkyl must be substituted with R_f wherein R_f is not hydroxy, sulphydryl or halogen;
and
when R₁ is C1alkyl then R_b cannot be carbamoyl, alkanoylamino, aroylamino, ureido, alkoxy carbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino,
20 amino, amidino or guanidino wherein each said R_b is linked to said R₁ via the nitrogen atom thereof.

- 25 Preferred compounds of the formula (Ia) are those wherein:

R_a is selected from the group consisting of H, alkyl and aryl;

- 30 R₁ is C1-8 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, pyranyl, thiopyranyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, or amino wherein R₁ is optionally substituted by one or more R_b;

- 40 R_b is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and

phenoxazinyl, C1-8 alkoxy, aryloxy, C1-8 alkoxycarbonyl, aryloxycarbonyl, C1-8
alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be
independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected
from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl,
5 thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group
consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl,
isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl,
pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl,
benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl,
10 quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8
alkanoylamino, aroylamino, C1-8 alkylthio wherein the sulfur atom may be
oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be
oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be
independently substituted by alkyl, aryl, heterocyclyl selected from the group
15 consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl
and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl,
pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl,
triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl,
indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl,
20 benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl,
carbazolyl, phenothiazinyl and phenoxazinyl, alkoxycarbonylamino,
aryloxycarbonylamino, C1-8 alkylcarbamoyloxy, arylcarbamoyloxy,
alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl,
25 amino wherein the nitrogen atom may be independently mono or di-substituted by
alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl,
piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl
selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,
thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl,
30 thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl,
benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl,
quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl
and phenoxazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and
guanidino, R_b may be further optionally substituted by one or more R_c;

35 R_c is selected from the group consisting of C1-8 alkyl, C3-6 cycloalkyl,
aryl, heterocyclyl selected from the group consisting of pyrrolidinyl,
piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl;
heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl,
oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl,
40 triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl,
pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl,
benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl,
quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl,
C1-8 alkoxy, aryloxy, halogen, hydroxy, oxo, carboxy, cyano, nitro,
45 amidino and guanidino;

R₃ is H, C1-8 alkyl, C3-7 cycloalkyl or aryl wherein R₃ is optionally substituted by one or more R_d;

- 5 R_d is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoxyazinyl, C1-8 alkoxy, aryloxy, alkanoyl, aroyl, C1-8 alkoxycarbonyl, aryloxycarbonyl, C1-8 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoxyazinyl, C1-8 alkanoylamino, aroylamino, C1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoxyazinyl, alkoxycarbonylamino, aryloxycarbonylamino, C1-8 alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoxyazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R_d may be further optionally substituted by one or more R_e;

R_e is selected from the group consisting of C1-8 alkyl, C3-6 cycloalkyl, aryl, arylalkyl, C1-8 alkoxy, aryloxy, arylalkoxy, aroyl, amino, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

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R₅ is H or alkyl;

R₆ is H, C1-8 alkyl, C3-7 cycloalkyl or aryl wherein R₆ is optionally substituted by one or more R_f,

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R_f is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoazinyl, C1-8 alkoxy, aryloxy, arylC1-8alkoxy, heteroarylC1-8alkoxy, C1-8 alkoxy carbonyl, aryloxycarbonyl, C1-8 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoazinyl, C1-8 alkanoylamino, aroylamino, C1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylC1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoazinyl, C1-8 alkylcarbamoyloxy, aryloxycarbonylamino, C1-8 alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl,

oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R_f may be further optionally substituted by one or more R_g;

R_g is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, 10 aryl optionally substituted by halogen, C1-3alkyl or C1-3alkoxy; heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, 15 oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoazinyl, C1-8 alkoxy, aryloxy, arylC1-8alkoxy, C1-8 alkoxycarbonyl, 20 aryloxycarbonyl, C1-8 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, 25 oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoazinyl, C1-8 alkanoylamino, aroylamino, C1-8 alkylthio wherein the sulfur atom 30 may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl 35 selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl or phenoazinyl, alkoxycarbonylamino, aryloxycarbonylamino, C1-8 alkylcarbamoyloxy, 40 alkylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl and arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, 45

5 piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoxyazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

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15 R_h is selected from the group consisting of C1-8 alkyl, aryl, C1-8 alkoxy carbonyl, aryloxy carbonyl, arylC1-8alkoxy carbonyl, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with a group selected from C1-8 alkyl, C3-7 cycloalkyl, aryl, arylC1-8alkyl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoxyazinyl, halogen, hydroxy, carboxy and cyano;

20 25 R_8 is a heteroaryl ring selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, indolizinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, indazolyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, tetrazolyl, purinyl, quinolizinyl, quinolinyl, isoquinolinyl, cinnolinyl, phthalazinyl, quinazolinyl, quinoxaliny, naphthyridinyl, pteridinyl, carbazolyl, acridinyl and phenazinyl, wherein any of the above R_8 can be optionally substituted by one or more R_j ;

30 35 40 45 R_j is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoxyazinyl, arylalkyl, alkoxy, aryloxy, arylalkoxy, alkoxy carbonyl, aryloxy carbonyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independantly mono or di-subsituted by alkyl, aryl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl,

oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoazinyl, alkanoylamino, 5 aroylamino, alkylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, arylalkylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, 10 piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiadiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, 15 quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoazinyl, alkoxy carbonylamino, aryloxy carbonylamino, C1-8 alkyl carbamoyloxy, aryl carbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, 20 piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiadiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, 25 quinoxaliny, carbazolyl, phenothiazinyl and phenoazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R_j may be further optionally substituted by one or more R_k;

30 R_k is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiadiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoazinyl, alkoxy, aryloxy, arylalkoxy, alkoxy carbonyl, aryloxy carbonyl, 35 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiadiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoazinyl, 40 alkoxy, aryloxy, arylalkoxy, alkoxy carbonyl, aryloxy carbonyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiadiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, 45 quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoazinyl,

benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl,
quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl,
phenothiazinyl and phenoxazinyl, alkanoylamino, aroylamino, alkylthio
wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, arylthio
5 wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, ureido
wherein either nitrogen atom may be independently substituted by alkyl,
aryl, heterocyclyl selected from the group consisting of pyrrolidinyl,
piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl,
10 heteroaryl selected from furanyl, thieryl, pyrrolyl, oxazolyl, thiazolyl,
imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl,
thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl,
isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl,
benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl,
15 quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl,
alkoxycarbonylamino, aryloxycarbonylamino, arylalkoxycarbonylamino,
arylalkoxycarbonylaminoalkyl, C1-8 alkylcarbamoyloxy,
arylcaramoyloxy, alkylsulfonylamino, arylsulfonylamino,
20 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom
may be independently mono or di-substituted by alkyl, aryl, heterocyclyl
selected from pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl,
piperazinyl and indolinyl, heteroaryl selected from the group consisting of
furanyl, thieryl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl,
25 isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl,
pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl,
benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl,
quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl,
phenothiazinyl and phenoxazinyl, halogen, hydroxy, oxo, carboxy, cyano,
nitro, amidino and guanidino, wherein R_k may be further optionally
substituted by R_l;

30 R_l is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, phenyl and benzyl;

and

35 X is O or S.

More preferred compounds of the formula (Ia) are those wherein:

40

Y is O or S;

45 R_l is C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group
consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, pyranyl,

thiopyranyl, piperazinyl and indolinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl or amino wherein R₁ is optionally substituted by one or more R_b;

- 5 R_b is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxy, aryloxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R_b may be further optionally substituted by one or more R_c;
- 10 R_c is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl, aryl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting
- 15 20 25 30 35 40 45

of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl and pyridinyl, C1-5 alkoxy, aryloxy, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

5 R₂ is H or C1-3 alkyl;

R₃ is H, C1-5 alkyl, C3-7 cycloalkyl or aryl, wherein R₃ is optionally substituted by one or more R_d;

10 R_d is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxy, aryloxy, C1-5 alkanoyle, aroyl, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of 15 pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 20 carbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R_d may be further optionally 25 substituted by one or more R_e;

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R_c is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl, aryl, arylalkyl, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, aroyl, amino, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

5

R₄ is H or C1-3 alkyl;

10 R₅ is H or C1-8 alkyl;

R₆ is H, C1-5 alkyl, C3-7 cycloalkyl or aryl wherein R₆ is optionally substituted by one or more R_f,

15 R_f is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, heteroarylC1-5alkoxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylC1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny, C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl,

5 thiomorpholiny, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R_f may be further optionally substituted by one or more R_g;

10 R_g is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, aryl optionally substituted by halogen, methyl or methoxy; heterocycl 15 selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholiny, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, C1-5 alkoxy carbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocycl 20 selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholiny, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, heterocycl 25 selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholiny, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxy carbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, 30 arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocycl 35 selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholiny, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxy carbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, 40 arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocycl 45 selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholiny, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and

quinoxalinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

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R_h is selected from the group consisting of C1-5 alkyl, aryl, C1-5 alkoxycarbonyl, aryloxycarbonyl, arylC1-5alkoxycarbonyl, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with a group selected from C1-5 alkyl, C3-7 cycloalkyl, aryl, arylC1-5alkyl, heterocyclcyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, halogen, hydroxy, carboxy and cyano;

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R_i is alkoxy, aryloxy or hydroxy;

R_g is a heteroaryl ring selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, indolizinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, indazolyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolizinyl, quinolinyl, isoquinolinyl, cinnolinyl, phthalazinyl, quinazolinyl, quinoxalinyl, naphthyridinyl, pteridinyl, carbazolyl, acridinyl and phenazinyl, wherein any of the above R_g can be optionally substituted by one or more R_j;

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R_j is selected from the group consisting of C1-8alkyl, C3-7cycloalkyl, aryl, heterocyclcyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl; arylC1-8alkyl, C1-8alkoxy, aryloxy, arylC1-8alkoxy, C1-8alkoxycarbonyl, aryloxycarbonyl, C1-8alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independantly mono or di-susbtituted by C1-8alkyl, aryl, heterocyclcyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8alkanoylamino, aroylamino, C1-8alkylthio wherein the

sulfur atom may be oxidised to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, arylC1-8alkylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, ureido wherein either
5 nitrogen atom may be independently substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoazinyl, alkoxy carbonylamino, aryloxy carbonylamino, C1-8 alkyl carbamoyloxy, aryl carbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R_j may be further optionally substituted by one or more R_k;

25 R_k is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoazinyl, C1-8 alkoxy, aryloxy, arylC1-8alkoxy, C1-8alkoxy carbonyl, aryloxycarbonyl, C1-8alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8alkyl, aryl, heterocyclyl selected from pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoazinyl, alkanoylamino, aroylamino, C1-8alkylthio wherein the sulfur atom may be oxidised to a sulfoxide or

sulfone, arylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-8alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, 5 piperazinyl and indolinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoazinyl, C1-8alkoxycarbonylamino, aryloxycarbonylamino, arylC1-8alkoxycarbonylamino, 10 arylalkoxycarbonylaminoC1-8alkyl, C1-8 alkylcarbamoyloxy, arylcarbamoyloxy, C1-8alkylsulfonylamino, arylsulfonylamino, C1-8alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-8alkyl, aryl, 15 heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, carbazolyl, phenothiazinyl and phenoazinyl, 20 halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, 25 wherein R_k may be further optionally substituted by R_i.

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Even more preferred compounds of the formula (Ia) are those wherein:

Y is O;

35 R₁ is C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, pyranyl and thiopyranyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, or amino 40 wherein R₁ is optionally substituted by one or more R_b;

45 R_b is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl,

benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl; C1-5 alkoxy, aryloxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl or aryl; C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy, cyano and nitro, R_b may be further optionally substituted by one or more R_c;

R_c is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl, aryl, C1-5 alkoxy, aryloxy, halogen, hydroxy, oxo, carboxy, and cyano;

R₂ is H or methyl;

R₃ is H, C1-5 alkyl, C3-7 cycloalkyl or phenyl, wherein R₃ is optionally substituted by one or more R_d;

R_d is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5 alkoxy, aryloxy, aroyl, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein

either nitrogen atom may be independently substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5 alkoxy carbonylamino, aryloxy carbonylamino, C1-5 alkyl carbamoyloxy, aryl carbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy and cyano, R_d may be further optionally substituted by one or more R_e;

R_e is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl, aryl, arylC1-5alkyl, C1-5 alkoxy, aryloxy, arylC1-3alkoxy, aroyl, amino, halogen, hydroxy, oxo, carboxy and cyano;

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R₄ is H or methyl;

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R₅ is H or C1-5 alkyl;

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R₆ is H, C1-5 alkyl, C3-7 cycloalkyl, phenyl or naphthyl wherein R₆ is optionally substituted by one or more R_f;

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R_f is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, pyridylC1-5alkoxy, thienylC1-5alkoxy, furanylC1-5alkoxy, C1-5 alkoxy carbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio

wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio
wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylC1-5
alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone,
ureido wherein either nitrogen atom may be independently substituted by C1-5
5 alkyl, aryl, heterocycl selected from the group consisting of piperidinyl,
morpholinyl and piperazinyl or heteroaryl selected from the group consisting of
furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl,
benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl,
10 quinolinyl and isoquinolinyl, C1-5 alkoxy carbonylamino, aryloxycarbonylamino,
C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino,
arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein
the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl,
15 aryl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl,
morpholinyl and piperazinyl or heteroaryl selected from the group consisting of
furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl,
benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl,
quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy and cyano, Rf may
be further optionally substituted by one or more R_g;

20 R_g is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl,
phenyl optionally substituted by halogen, methyl or methoxy; naphthyl
optionally substituted by halogen, methyl or methoxy; heterocycl
selected from the group consisting of pyrrolidinyl, piperidinyl,
morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl
25 selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,
thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl,
pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl,
benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and
quinoxalinyl, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, C1-5
30 alkoxy carbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl
wherein the nitrogen atom may be independently mono or di-substituted
by C1-5 alkyl, aryl, heterocycl selected from the group consisting of
piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the
group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl,
35 imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl,
benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl,
C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom
may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom
may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen
40 atom may be independently substituted by C1-5 alkyl, aryl, heterocycl
selected from the group consisting of piperidinyl, morpholinyl and
piperazinyl or heteroaryl selected from the group consisting of furanyl,
thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl,
benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl,
45 quinolinyl, isoquinolinyl, C1-5 alkoxy carbonylamino,
aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5

alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy and cyano;

10

R_h is selected from the group consisting of C1-5 alkyl, phenyl, naphthyl, C1-5 alkoxycarbonyl, aryloxycarbonyl, arylC1-3alkoxycarbonyl, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with a group selected from C1-5 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, arylC1-3alkyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, carboxy and cyano;

25 Z is O or S;

R_g is a heteroaryl ring selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, indolizinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, indazolyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolizinyl, quinolinyl, isoquinolinyl, cinnolinyl, phthalazinyl, quinazolinyl, quinoxaliny, naphthyridinyl, pteridinyl, carbazolyl, acridinyl and phenazinyl, wherein any of the above R_g can be optionally substituted by one or more groups of the formula R_j;

35

R_j is selected from the group consisting of C1-5alkyl, C3-6cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, arylC1-5alkyl, C1-5alkoxy, aryloxy, arylC1-5alkoxy, C1-Salkoxycarbonyl, aryloxycarbonyl, C1-5alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independantly mono or di-susbtituted by C1-5alkyl, aryl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl, heteroaryl selected from furanyl, thienyl, pyrrolyl,

oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5alkanoylamino, aroylamino, C1-5alkylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, arylC1-5alkylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5alkylsulfonylamino, arylsulfonylamino, C1-5alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-susbtituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, wherein R_j may be further optionally substituted by one or more R_k;

R_k is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, tetrazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, C1-3 alkoxy, aryloxy, arylC1-3alkoxy, C1-3alkoxycarbonyl, aryloxycarbonyl, C1-3alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independantly mono or di-susbtituted by C1-3 alkyl, aryl, heterocyclyl selected from the group consisting of morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, and pyridinyl, C1-3alkanoylamino, aroylamino, C1-3alkylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-3alkyl, phenyl, naphthyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl and pyridinyl, C1-3alkoxycarbonylamino, aryloxycarbonylamino, arylC1-3alkoxycarbonylamino, benzyloxycarbonylaminoC1-5alkyl, C1-3 alkylcarbamoyloxy, arylcarbamoyloxy, C1-3alkylsulfonylamino, arylsulfonylamino, C1-3alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-susbtituted by C1-3alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the

group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy, cyano and nitro, wherein R_k may be further optionally substituted by R_i;

R_i is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl and phenyl.

10

Yet even more preferred compounds of the formula (Ia) are those wherein:

15

R_i is C1-5 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl, piperazinyl, pyranyl and thiopyranyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, or amino, wherein R_i is optionally substituted by one or more R_b;

25

R_b is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-3 alkoxy, phenoxy, C1-3

30

alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5alkyl, phenyl or naphthyl; C1-5

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alkoxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,

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thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl,

45

halogen, hydroxy, oxo, carboxy and cyano, R_b may be further optionally substituted by one or more R_c;

5 R_c is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, aryl, C1-3 alkoxy, phenoxy, halogen, hydroxy, oxo, carboxy and cyano;

R₂ is H;

10 R₃ is C1-5 alkyl, C3-6 cycloalkyl or phenyl, wherein R₃ is optionally substituted by one or more R_d;

15 R_d is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, quinolinyl andisoquinolinyl, C1-5 alkoxy, phenoxy, aroyl, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, C1-5 alkanoylamino, aroylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, phenylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-3 alkyl, phenyl or heteroaryl selected the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, C1-5 alkoxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, phenyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, halogen, hydroxy, oxo, carboxy and cyano, R_d may be further optionally substituted by one or more R_e;

35 R_e is selected from the group consisting of C1-5 alkyl, C5-6 cycloalkyl, phenyl, naphthyl, arylC1-3alkyl, C1-5 alkoxy, phenoxy, arylC1-3alkoxy, aroyl, amino, halogen, hydroxy, oxo, carboxy and cyano;

40 wherein the configuration at the stereocenter defined by R₂ and R₃ and the carbon they are attached to is L;

45 R₄ is H;

R₅ is H or C1-3 alkyl;

- 5 R₆ is H, C1-5 alkyl, C3-6 cycloalkyl or phenyl, wherein R₆ is optionally substituted by one or more R_f;

R_f is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5 alkoxy, aryloxy, arylC1-3alkoxy, pyridylC1-5alkoxy, thienylC1-5alkoxy, furanylC1-5alkoxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, C1-5 alkanoylamino, aroylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylC1-3alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl or phenyl; C1-5 alkoxycarbonylamino, C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, halogen, hydroxy, oxo, carboxy and cyano, R_f may be further optionally substituted by one or more R_g;

R_g is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl optionally substituted by halogen, methyl or methoxy; heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, pyrimidinyl, pyrazinyl and indolyl, C1-5 alkoxy, aryloxy, arylC1-3alkoxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or aryl; C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl or aryl; C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5

alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or aryl; halogen, hydroxy, oxo, carboxy and cyano;

5

R₄ is selected from the group consisting of C1-5 alkyl, phenyl, C1-5 alkoxy carbonyl, aryloxy carbonyl, arylC1-3alkoxy carbonyl, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with C1-5 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, arylC1-3alkyl, halogen, hydroxy, carboxy and cyano;

10 wherein Z is O;

15

R₈ is a heteroaryl ring selected from the group consisting of oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, wherein any of the above R₈ can be optionally substituted by one or more R_j;

20 R_j is selected from the group consisting of C1-5 alkyl, C5-6 cycloalkyl, phenyl, naphthyl, pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, furanyl, thienyl, pyrrolyl, tetrazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, arylC1-3alkyl, C1-3alkoxy, aryloxy, arylC1-3alkoxy, C1-3alkoxy carbonyl, aryloxy carbonyl, C1-3alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-subsituted by C1-3alkyl, phenyl, naphthyl, piperidinyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl; C1-3alkanoylamino, aroylamino, C1-3alkylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, arylC1-3alkylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-3 alkyl, phenyl, naphthyl, piperidinyl, morpholinyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl; C1-3 alkoxy carbonylamino, aryloxy carbonylamino, C1-3 alkyl carbamoyloxy, aryl carbamoyloxy, C1-3alkylsulfonylamino, arylsulfonylamino, C1-3alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-subsituted by C1-3 alkyl, phenyl, naphthyl, piperidinyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl,

benzoxazolyl, quinolinyl and isoquinolinyl; halogen, hydroxy, oxo, carboxy, cyano and nitro, R_j may be further optionally substituted by one or more R_k;

R_k is selected from the group consisting of methyl, C5-6 cycloalkyl, phenyl, pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, furanyl, thienyl, pyrrolyl, tetrazolyl, pyridinyl, pyrimidinyl, C1-3 alkoxy, phenoxy, benzyloxy, methoxycarbonyl, acetyloxy, benzoyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, phenyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl or pyridinyl; acetyl amino, benzoyl amino, methylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by methyl, phenyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl or pyridinyl; arylC1-3alkoxycarbonylamino, benzyloxycarbonylaminoC1-5alkyl, methylcarbamoyloxy, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3alkyl, phenyl, naphthyl, pyrrolidinyl, piperidinyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, pyrimidinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl or isoquinolinyl, halogen, hydroxy, oxo, carboxy, cyano and nitro, wherein R_k may be further optionally substituted by R_j;

R_j is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl and phenyl.

25

30 Still yet even more preferred compounds of the formula (Ia) are those wherein:

R₁ is C1-3 alkyl, C5-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl, piperazinyl, pyranyl and thiopyranyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, or amino, wherein R₁ is optionally substituted by one or more R_b;

R_b is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-3 alkoxy, C1-3 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, phenyl or heteroaryl selected from the group consisting of pyrrolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl,

benzimidazolyl and benzthiazolyl; C1-5 alkanoylamino, aroylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-3alkyl or phenyl; C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3alkyl, phenyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of pyrrolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl; halogen, hydroxy, oxo, carboxy and cyano, R_b may be further optionally substituted by one or more R_c;

R_c is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, C1-3 alkoxy, halogen and hydroxy;

15

R₃ is C1-5 alkyl, C5-6 cycloalkyl or phenyl wherein R₃ is optionally substituted by one or more R_d;

20

R_d is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, 4-piperidinyl, 4-morpholinyl, piperazinyl, furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-5 alkoxy, phenoxy, aroyl, C1-5 alkoxy carbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or phenyl; C1-5 alkanoylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-3 alkyl or phenyl; C1-5 alkoxy carbonylamino, C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; halogen, hydroxy, oxo, carboxy and cyano, R_d may be further optionally substituted by one or more R_e;

35

R_e is selected from the group consisting of C1-5 alkyl, C5-6 cycloalkyl, phenyl, benzyl, C1-5 alkoxy, phenoxy, benzyloxy, aroyl, halogen, hydroxy, oxo, carboxy and cyano;

R₆ is H, C1-5 alkyl or phenyl wherein R₆ is optionally substituted by one or more R_f;

40

R_f is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-3 alkoxy, benzyloxy, pyridyl, C1-3alkoxy, thienylC1-3alkoxy, furanylC1-3alkoxy, C1-3 alkoxy carbonyl, phenoxyoxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; C1-5 alkanoylamino, aroylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur

atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl or phenyl; C1-3 alkoxycarbonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or phenyl; halogen, hydroxy, oxo, carboxy and cyano, R_f may be further optionally substituted by one or more R_g;

5

R_g is selected from the group consisting of C1-3 alkyl, phenyl optionally substituted by halogen, methyl or methoxy; heterocycll selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl and pyridinyl, C1-3 alkoxy, aryloxy, benzyloxy, C1-5 alkoxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or phenyl; C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl or phenyl; C1-5 alkoxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-3 alkylsulfonylamino, arylsulfonylamino, C1-3 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; halogen, hydroxy, oxo, carboxy and cyano;

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R_h is selected from the group consisting of C1-3 alkyl, phenyl, C1-3 alkoxycarbonyl, phenoxyoxycarbonyl, benzyloxy, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with C1-5 alkyl, phenyl, benzyl, halogen, hydroxy, carboxy and cyano;

R_g is a heteroaryl ring selected from the group consisting of oxazolyl, thiazolyl, imidazolyl, pyrazolyl, pyridyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, wherein any of the above R₈ can be optionally substituted by one or more R_j;

R_j is selected from the group consisting of C1-5 alkyl, C5-6 cycloalkyl, phenyl, naphthyl, pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, furanyl, thienyl, pyrrolyl, tetrazolyl, pyridinyl, pyrimidinyl, benzyl, C1-3alkoxy, phenoxy, benzyloxy, C1-3alkoxycarbonyl, acetoxy, benzoyloxy, carbamoyl wherein the nitrogen atom may be independantly mono or di-susbtituted by methyl, phenyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl and pyridinyl; acetylarnino, benzoylamino, methylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by methyl, phenyl, thiazolyl, imidazolyl and pyridinyl; C1-3 alkoxycarbonylamino, C1-3 alkylcarbamoyloxy, arylcarbamoyloxy, C1-

3alkylsulfonylamino; arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by methyl, phenyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl and pyridinyl; halogen, hydroxy, carboxy, cyano and nitro, R_j may be further optionally substituted by one or more R_k;

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R_k is selected from the group consisting of methyl, C5-6 cycloalkyl, phenyl, pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, furanyl, thienyl, pyrrolyl, pyridinyl, C1-3 alkoxy, phenoxy, benzyloxy, methoxycarbonyl, acetoxy, benzoyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by methyl, phenyl, furanyl, thienyl; acetyl, amino, benzoylamino, methylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by methyl, phenyl, furanyl, thienyl, pyrrolyl, oxazolyl and thiazolyl, benzyloxycarbonylamino, benzyloxycarbonylaminoC1-Salkyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3alkyl, phenyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl and pyridinyl, halogen, hydroxy, carboxy, cyano and nitro, wherein R_k may be further optionally substituted by R_i;

R_i is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl and phenyl.

Even much more preferred compounds of the formula (Ia) are those wherein:

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R₁ is C5-6 cycloalkyl, phenyl, naphthyl, piperidinyl, morpholinyl, piperazinyl, furanyl, thienyl, pyrrolyl, pyranyl, thiopyranyl or amino wherein R₁ is optionally substituted by one or more R_b;

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R_b is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl, furanyl, thienyl, pyrrolyl, imidazolyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, C1-3 alkoxy, C1-3 alkoxycarbonyl, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; C1-5 alkanoylamino, aroylamino, ureido wherein either nitrogen atom may be independently substituted by C1-3alkyl or phenyl; C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3alkyl or phenyl;, halogen, hydroxy, oxo, carboxy and cyano, R_b may be further optionally substituted by one or more R_c;

R_c is selected from the group consisting of C1-3 alkyl, C1-3 alkoxy, halogen and hydroxy;

5 R_d is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, 4-piperidinyl, furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-3alkoxy, C1-Salkoxycarbonyl, C1-Salkanoyloxy, benzyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3alkyl or phenyl; C1-Salkanoylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, C1-3alkoxycarbonylamino, C1-3alkylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, halogen, hydroxy, oxo, carboxy and cyano, R_d may be further optionally substituted by one or more R_e;

10 R_e is selected from the group consisting of C1-3 alkyl, phenyl, benzyl, C1-3 alkoxy, phenoxy, benzyloxy, benzoyl, halogen, hydroxy, oxo, carboxy and cyano;

15 R_s is H or methyl;

20 R₆ is C1-5 alkyl or phenyl, wherein R₆ is optionally substituted by one or more groups of the formula R_f,

25 R_f is selected from the group consisting of methyl, C3-6 cycloalkyl, phenyl, naphthyl, furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-3 alkoxy, benzyloxy, C1-5 alkanoylamino, aroylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, C1-3 alkoxy carbonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or phenyl; halogen, hydroxy, oxo, carboxy and cyano, R_f may be further optionally substituted by one or more R_g;

35 R_g is selected from the group consisting of C1-3 alkyl, phenyl optionally substituted by halogen or methyl; C1-3 alkoxy, aryloxy, benzyloxy, C1-3 alkoxy carbonyl, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; C1-5 alkanoylamino, aroylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; halogen, hydroxy, oxo, carboxy and cyano;

40 R_h is selected from the group consisting of C1-3 alkyl, phenyl, C1-3 alkoxy carbonyl, benzyloxy and carboxy;

R_8 is a heteroaryl ring selected from the group consisting of oxazolyl, thiazolyl, imidazolyl, pyrazolyl, pyridyl, benzimidazolyl, benzthiazolyland benzoxazolyl, wherein any of the above R_8 can be optionally substituted by one or more R_j ;

- 5 R_j is selected from the group consisting of C1-5 alkyl, cyclohexyl, phenyl, piperidinyl, furanyl, thienyl, pyridinyl, benzyl, methoxy, phenoxy, benzyloxy, methoxycarbonyl, acetyloxy, benzyloxy, carbamoyl wherein the nitrogen atom may be independantly mono or di-susbsituted by methyl, phenyl, furanyl, thienyl; acetylarnino, benzoylamino, ureido wherein either nitrogen atom may be
- 10 independently substituted by methyl or phenyl; methoxycarbonylamino, C1-3 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-susbsituted by methyl, phenyl, furanyl or thienyl; halogen, hydroxy, carboxy and cyano, R_j may be further optionally substituted by one or more R_k ;
- 15 R_k is selected from the group consisting of methyl, C5-6 cycloalkyl, phenyl, piperidinyl, piperazinyl, furanyl, thienyl, C1-3 alkoxy, phenoxy, benzyloxy, methoxycarbonyl, acetyloxy, benzyloxy, carbamoyl wherein the nitrogen atom may be independantly mono or di-susbsituted by
- 20 methyl or phenyl; acetylarnino, benzoylamino, ureido wherein either nitrogen atom may be independently substituted by methyl or phenyl; benzyloxycarbonylamino, benzyloxycarbonylamino C1-5alkyl, amino wherein the nitrogen atom may be independently mono or di-susbsituted by C1-3 alkyl, phenyl, furanyl, or thienyl; halogen, hydroxy, carboxy, cyano and nitro, wherein R_k may be further optionally substituted by R_l ;
- 25 R_l is selected from the group consisting of methyl, C3-6 cycloalkyl and phenyl.

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Yet even more preferred compounds of the formula (Ia) are those wherein:

- 35 A is -C(O)- or -SO₂-;

R_1 is cyclohexyl, phenyl, naphthyl, piperidinyl, morpholinyl, piperazinyl, pyranyl, thiopyranyl or amino, wherein R_1 is optionally substituted by one or more R_b ;

- 40 R_b is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl, furanyl, thienyl, pyrrolyl, imidazolyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, C1-3 alkoxy, C1-3 alkoxy carbonyl, carbamoyl wherein the nitrogen atom may be independently mono or di- substituted by C1-3 alkyl or phenyl; C1-5 alkanoylamino, aroylamino, C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be
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independently mono or di-substituted by C1-3 alkyl; halogen, hydroxy, oxo, carboxy and cyano, R_b may be further optionally substituted by one or more R_c;

5 R_c is selected from the group consisting of C1-3 alkoxy, halogen and hydroxy;

R₃ is C1-5 alkyl or C5-6 cycloalkyl, wherein R₃ is optionally substituted by one or more R_d;

10 R_d is selected from the group consisting of methyl, C3-6 cycloalkyl, phenyl, thienyl, imidazolyl, pyridinyl, indolyl, C1-4 alkoxy, C1-5 alkanoylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, halogen, hydroxy, oxo, carboxy and cyano, R_d may be further optionally substituted by one or more R_e;

15 R_e is selected from the group consisting of methyl, phenyl, benzyl, methoxy, phenoxy, benzyloxy, benzoyl, halogen and hydroxy;

20 R_f is selected from the group consisting of C3-6 cycloalkyl, phenyl, naphthyl, thienyl, imidazolyl, pyridinyl, indolyl, methoxy, benzyloxy, C1-3 alkanoylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, methoxycarbonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl; halogen, hydroxy, carboxy and cyano, R_f may be further optionally substituted by one or more R_g;

25 R_g is selected from the group consisting of methyl, phenyl optionally substituted by halogen or methyl; methoxy, phenoxy, benzyloxy, methoxycarbonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; halogen, hydroxy and carboxy;

30 R₈ is a heteroaryl ring selected from the group consisting of oxazolyl, thiazolyl, imidazolyl, pyridyl, benzthiazolyl and benzoxazolyl, wherein any of the above R₈ can be optionally substituted by one or more R_j;

35 R_j is selected from the group consisting of C1-5 alkyl, phenyl, furanyl, thienyl, piperidinyl, pyridinyl, benzyl, methoxy, methoxycarbonyl, acetyloxy, benzyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by methyl or phenyl; acetylarnino, benzoylamino, ureido wherein either nitrogen atom may be independently substituted by methyl or phenyl; methoxycarbonylamino, amino wherein the nitrogen atom may be independently mono or di-susbsituted by methyl, phenyl; halogen, hydroxy, carboxy and cyano, R_j may be further optionally substituted by one or more R_k; and

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R_k is selected from the group consisting of methyl, C5-6 cycloalkyl, phenyl, piperidinyl, methoxy, phenoxy, benzyloxy, methoxycarbonyl, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by methyl or phenyl; ureido wherein either nitrogen atom may be independently substituted by methyl or phenyl; benzyloxycarbonylamino, benzyloxycarbonylaminoC1-5alkyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3alkyl, phenyl, furanyl and thieryl; halogen, hydroxy, carboxy, cyano and nitro, wherein R_k may be further optionally substituted by R_l;

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R_l is selected from the group consisting of methyl and phenyl.

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Penultimately preferred compounds of the formula (Ia) are those wherein:

R₁ is cyclohexyl, phenyl, naphthyl, piperidinyl, morpholinyl, piperazinyl, pyranyl or thiopyranyl, wherein R₁ is optionally substituted by one or more R_b;

20 R_b is selected from the group consisting of, pyrrolyl, imidazolyl, indolyl, benzimidazolyl, methoxy, methoxycarbonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl; halogen, hydroxy and carboxy, R_b may be further optionally substituted by one or more R_c;

25

R_c is selected from the group consisting of methoxy, halogen and hydroxy;

30

R_d is selected from the group consisting of methyl, C3-6 cycloalkyl, phenyl, C1-4 alkoxy, C1-3 alkanoylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, halogen, hydroxy, oxo, carboxy and cyano, R_d may be further optionally substituted by one or more R_e;

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R_e is selected from the group consisting of methyl, phenyl, methoxy, halogen and hydroxy;

R_f is H;

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R_f is selected from the group consisting of C5-6 cycloalkyl, phenyl, naphthyl, thieryl, indolyl, methoxy, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, methoxycarbonylamino, halogen, hydroxy, carboxy and cyano, R_f may be further optionally substituted by one or more R_g;

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R_g is selected from the group consisting of methyl, phenyl optionally substituted by halogen; methoxy, phenoxy, benzyloxy, methoxycarbonyl, halogen, hydroxy and carboxy;

5 R₈ is a heteroaryl ring selected from the group consisting of oxazolyl, thiazolyl, pyridyl, benzthiazolyl and benzoxazolyl, wherein any of the above R₈ can be optionally substituted by one or more R_j;

10 R_j is selected from the group consisting of C1-5 alkyl, phenyl, piperidinyl, pyridinyl, benzyl, methoxy, methoxycarbonyl, acetyloxy, benzyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by methyl or phenyl; methoxycarbonylamino, halogen, hydroxy and carboxy, R_j may be further optionally substituted by one or more R_k;

15 R_k is selected from the group consisting of methyl, C5-6 cycloalkyl, phenyl, piperidinyl, methoxy, methoxycarbonyl, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by methyl or phenyl; benzyloxycarbonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by methyl or phenyl; halogen, hydroxy and carboxy.

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Ultimately preferred compounds of the formula (Ia) are those wherein:

25 R₁ is phenyl or 4-morpholinyl, wherein R₁ is optionally substituted by one or more R_b;

R_b is selected from the group consisting of benzimidazolyl, methoxy and dimethylamino, R_b may be further optionally substituted by a halogen atom;

30 R₃ is C1-5 alkyl wherein R₃ is optionally substituted by one or more R_d;

R_d is selected from the group consisting of C3-6 cycloalkyl and phenyl, R_d may be further optionally substituted by one or more R_e;

35 R_e is selected from the group consisting of methyl and halogen;

R₆ is C1-5 alkyl optionally substituted by one or more R_f;

40 R_f is selected from the group consisting of C5-6 cycloalkyl, phenyl, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, and halogen, R_f may be further optionally substituted by one or more R_g;

R_g is selected from the group consisting of methyl, methoxy, methoxycarbonyl, halogen and hydroxy;

R₈ is a heteroaryl ring selected from the group consisting of oxazolyl, pyridyl, benzthiazolyl and benzoazolyl, wherein any of the above R₈ can be optionally substituted by one or more R_j;

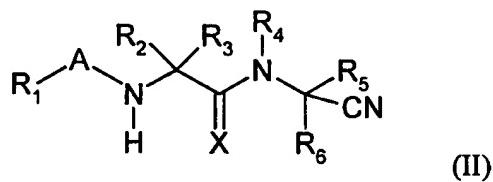
5 R_j is selected from the group consisting of C1-5 alkyl, phenyl, pyridinyl, piperidinyl, methoxycarbonyl, carbamoyl wherein the nitrogen atom may be independantly mono or disubstituted by methyl or phenyl; methoxycarbonylamino and halogen, R_j may be further optionally substituted by one or more R_k;

10 R_k is selected from the group consisting of methyl, C5-6 cycloalkyl, phenyl, methoxycarbonyl, carbamoyl, benzyloxycarbonylamino and halogen.

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The invention also provides novel compounds of the formula (II):

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wherein:

A is -C(Y)- or -SO₂-

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Y is O, S or NR_a wherein R_a is selected from the group consisting of H, alkyl, aryl, alkoxy, aryloxy, alkylamino and arylamino;

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R₁ is alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl or amino wherein R₁ is optionally substituted by one or more R_b;

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R_b is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkoxy, aryloxy, alkanoyl, aroyl, alkoxycarbonyl, aryloxycarbonyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a

sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocycll or heteroaryl, alkoxycarbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocycll or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino; R_b may be further optionally substituted by one or more R_c;

10 R_c is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocycll, heteroaryl, arylalkyl, alkoxy, aryloxy, arylalkoxy, alkanoyl, aroyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocycll or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

15 R₂ is H or alkyl;

R₃ is H, alkyl, cycloalkyl, aryl, heterocycll or heteroaryl, wherein R₃ is optionally substituted by one or more R_d;

20 R_d is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocycll, heteroaryl, alkoxy, aryloxy, arylalkoxy, alkoxycarbonyl, aryloxycarbonyl, alkanoyl, aroyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocycll or heteroaryl, alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocycll or heteroaryl, alkoxycarbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocycll or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R_d may be further optionally substituted by one or more R_e;

35 R_e is selected from the group consisting of alkyl, cycloalkyl, aryl, arylalkyl, alkoxy, aryloxy, arylalkoxy, alkanoyl, aroyl, amino, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

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R₄ is H or alkyl;

45 R₅ is H or alkyl;

R₆ is H, alkyl, cycloalkyl, aryl, heterocyclyl, aryl, heteroaryl or cyano, wherein R₆ is optionally substituted by one or more R_f,

5 R_f is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkoxy, aryloxy, arylalkoxy, alkanoyl, aroyl, alkoxycarbonyl, aryloxycarbonyl, alkanoyloxy, aroyloxy, heteroarylalkoxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkanoylamino, aroylamino, alkylcarbamoyl, 10 arylcaramoyl, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylalkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkoxycarbonylamino, 15 aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R_f may be further optionally substituted by one or 20 more R_g;

25 R_g is selected from the group consisting of alkyl, cycloalkyl, aryl optionally substituted by one or more groups selected from halogen, methyl or methoxy, heterocyclyl, heteroaryl, alkoxy, aryloxy, arylalkoxy, alkoxycarbonyl, aryloxycarbonyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkanoylamino, aroylamino, alkylcarbamoyl, arylcarbamoyl, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkoxycarbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

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40 or R₅ together with R₆ form a 3 to 6 membered carbocyclic ring, the carbocyclic ring being optionally substituted with one or more R_h;

45 R_h is selected from the group consisting of alkyl, aryl, alkoxycarbonyl, aryloxycarbonyl, arylalkoxycarbonyl, carbamoyl wherein the nitrogen atom may

be optionally mono or di-substituted with a group selected from alkyl, cycloalkyl, aryl, arylalkyl, heterocyclyl, heteroaryl, halogen, hydroxy, carboxy and cyano;

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X is O, S or N-OH;

with the proviso that when Y is O and R₆ is arylalkyl or heteroarylalkyl then R₁ cannot be alkyl, cycloalkyl, aryl, heteroaryl, cycloalkyl-alkyl, aryl-alkyl or aryl-cycloalkyl.

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15 Preferred compounds of the formula (II) are those wherein:

Y is O, S or NR_a, wherein R_a is H, alkyl or aryl;

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R₁ is C1-8alkyl, C3-7cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, indolinyl, pyranyl and thiopyranyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl, phenoxazinyl, and amino wherein R₁ is optionally substituted by one or more R₅:

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R_b is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl or phenoxyazinyl, C1-8 alkoxy, aryloxy, C1-8 alkoxycarbonyl, aryloxycarbonyl, C1-8 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl.

carbazolyl, phenothiazinyl and phenoazinyl, C1-8 alkanoylamino, aroylamino, C1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl or phenoazinyl, alkoxy carbonylamino, aryloxy carbonylamino, alkyl carbamoyloxy, aryl carbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, pyrazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino, guanidino; R_b may be further optionally substituted by one or more R_c;

R_c is selected from the group consisting of C1-8 alkyl, C3-6 cycloalkyl, aryl, C1-8 alkoxy, aryloxy, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

R₃ is H, C1-8 alkyl, C3-7 cycloalkyl, aryl wherein R₃ is optionally substituted by one or more R_d;

R_d is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoazinyl, C1-8 alkoxy, aryloxy, alkanoyl, aroyl, C1-8 alkoxy carbonyl, aryloxy carbonyl, C1-8 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl,

thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkanoylamino, aroylamino, C1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, alkoxy carbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino, guanidino, R_d may be further optionally substituted by one or more R_e;

R_e is selected from the group consisting of C1-8 alkyl, C3-6 cycloalkyl, aryl, arylalkyl, C1-8 alkoxy, aryloxy, arylalkoxy, aroyl, amino, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

R₆ is H, C1-8 alkyl, C3-7 cycloalkyl, aryl or cyano, wherein R₆ is optionally substituted by one or more R_f;

R_f is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8

alkoxy, aryloxy, arylC1-8alkoxy, heteroarylC1-8alkoxy, C1-8 alkoxy carbonyl, aryloxycarbonyl, C1-8 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxyazinyl, C1-8 alkanoylamino, aroylamino, C1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxyazinyl, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxyazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R_f may be further optionally substituted by one or more R_g;

R_g is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl optionally substituted by one or more groups selected from halogen, methyl or methoxy, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxyazinyl, C1-8 alkoxy, aryloxy, arylC1-8alkoxy, C1-8

alkoxycarbonyl, aryloxycarbonyl, C1-8 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoazinyl, C1-8 alkanoylamino, aroylamino, C1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoazinyl, alkoxycarbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino, and guanidino;

R_h is selected from the group consisting of C1-8 alkyl, aryl, C1-8 alkoxycarbonyl, aryloxycarbonyl, arylC1-8alkoxycarbonyl, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with a group selected from C1-8 alkyl, C3-7 cycloalkyl, aryl, arylC1-8alkyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl,

benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoazinyl, halogen, hydroxy, carboxy, and cyano; and

5 X is O or S.

More preferred compounds of the formula (II) are those wherein:

10

Y is O or S;

15 R₁ is C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, indolinyl, pyranyl and thiopyranyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny or amino;

20 wherein R₁ is optionally substituted by one or more R_b;

25 R_b is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny, C1-5 alkoxy, aryloxy, C1-5
30 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny, C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5

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alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, 5 arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R_b may be further optionally substituted by one or more R_c;

10 R_c is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl, aryl, C1-5 alkoxy, aryloxy, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

15 R₂ is H or C1-3 alkyl;

R₃ is H, C1-5 alkyl, C3-7 cycloalkyl, aryl wherein R₃ is optionally substituted by one or more R_d;

20 R_d is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxy, aryloxy, C1-5 alkanoyle, aroyl, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl,

arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, 5 pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R_d may be further optionally substituted by one or more R_e;

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R_e is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl, aryl, arylalkyl, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, aroyl, amino, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

15

R₄ is H or C1-3 alkyl

20 R₅ is H or C1-8 alkyl

R₆ is H, C1-5 alkyl, C3-7 cycloalkyl, aryl or cyano, wherein R₆ is optionally substituted by one or more R_f;

25

R_f is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, aryl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, heteroarylC1-5alkoxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl,

5 piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, 10 aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, halogen, hydroxy, oxo, carboxy, 15 cyano, nitro, amidino and guanidino, R_f may be further optionally substituted by one or more R_g:

20 R_g is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, aryl optionally substituted by one or more groups selected from halogen, methyl or methoxy, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, C1-5 25 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, 30 heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 35 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 40 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 45 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino,

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arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino
wherein the nitrogen atom may be independently mono or di-substituted
by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of
pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and
indolinyl, or heteroaryl selected from the group consisting of furanyl,
thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl,
pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl,
benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and
10 quinoxalinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and
guanidino;

15

R_h is selected from the group consisting of C1-5 alkyl, aryl, C1-5 alkoxycarbonyl,
aryloxycarbonyl, arylC1-5alkoxycarbonyl, carbamoyl wherein the nitrogen atom
may be optionally mono or di-substituted with a group selected from C1-5 alkyl,
C3-7 cycloalkyl, aryl, arylC1-5alkyl, heterocyclyl selected from the group
consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl
and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl,
20 pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl,
pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl,
benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, halogen,
hydroxy, carboxy and cyano.

25

Even more preferred compounds of the formula (II) are those wherein:

Y is O;

30

R_1 is C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group
consisting of piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, pyranyl and
thiopyranyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl,
oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl,
35 benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl; or amino wherein R_1 is
optionally substituted by one or more R_b ;

40

R_b is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, phenyl,
naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl,
piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl
selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,
thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl,
benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 alkoxy,
aryloxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy,
45 carbamoyl wherein the nitrogen atom may be independently mono or di-
substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group

consisting of pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl or aryl, C1-5 alkoxy carbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy, cyano and nitro, R_b may be further optionally substituted by one or more R_c;

R_c is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl, aryl, C1-5 alkoxy, aryloxy, halogen, hydroxy, oxo, carboxy and cyano;

R₂ is H or methyl;

R₃ is H, C1-5 alkyl, C3-7 cycloalkyl or phenyl wherein R₃ is optionally substituted by one or more R_d;

R_d is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 alkoxy, aryloxy, aroyl, C1-5 alkoxy carbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl,

benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5
alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy,
arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5
alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be
5 independently mono or di-substituted by C1-5 alkyl, phenyl, naphthyl,
heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and
piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl,
pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl,
10 benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl,
halogen, hydroxy, oxo, carboxy and cyano, R_d may be further optionally
substituted by one or more R_e;

R_e is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl,
15 aryl, arylC1-5alkyl, C1-5 alkoxy, aryloxy, arylC1-3alkoxy, aroyl, amino,
halogen, hydroxy, oxo, carboxy and cyano;

R₄ is H or methyl;

20 R₅ is H or C1-5 alkyl;

R₆ is H, C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl or cyano, wherein R₆ is optionally
25 substituted by one or more R_f.

R_f is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, phenyl,
naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl,
piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl
selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,
30 thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl,
indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl,
isoquinolinyl, quinazolinyl and quinoxaliny, C1-5 alkoxy, aryloxy, arylC1-
5alkoxy, heteroarylC1-5alkoxy, C1-5 alkoxy carbonyl, aryloxycarbonyl, C1-5
35 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be
independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected
from the group consisting of piperidinyl, morpholinyl and piperazinyl or
heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl,
oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl,
benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino,
40 aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a
sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a
sulfoxide or sulfone, arylC1-5 alkylthio wherein the sulfur atom may be oxidized
to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be
45 independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from the
group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl
selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,

thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl,
benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5
alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy,
arylcaramoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5
5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be
independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected
from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and
piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl,
10 pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl,
benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl,
halogen, hydroxy, oxo, carboxy and cyano, R_f may be further optionally
substituted by one or more R_g;

15 R_g is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl,
phenyl optionally substituted by one or more groups selected from
halogen, methyl or methoxy, naphthyl optionally substituted by one or
more groups selected from halogen, methyl or methoxy, heterocyclyl
selected from the group consisting of pyrrolidinyl, piperidinyl,
morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl
20 selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,
thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl,
pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl,
benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny,
C1-5 alkoxy, aryloxy, arylC1-5alkoxy, C1-5 alkoxycarbonyl,
aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the
25 nitrogen atom may be independently mono or di-substituted by C1-5 alkyl,
aryl, heterocyclyl selected from the group consisting of piperidinyl,
morpholinyl and piperazinyl or heteroaryl selected from the group
consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl,
30 pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl,
benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino,
aroyleamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a
sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a
35 sulfoxide or sulfone, ureido wherein either nitrogen atom may be
independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from
the group consisting of piperidinyl, morpholinyl and piperazinyl or
heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl,
oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl,
benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl,
40 C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5
alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino,
arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino
wherein the nitrogen atom may be independently mono or di-substituted
by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of
45 pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl or heteroaryl
selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,

thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy and cyano;

5

R_b is selected from the group consisting of C1-5 alkyl, phenyl, naphthyl, C1-5 alkoxycarbonyl, aryloxycarbonyl, arylC1-3alkoxycarbonyl, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with a group selected from C1-5 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, arylC1-3alkyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, carboxy and cyano; and

10

15

X is O.

20

Yet even more preferred compounds of the formula (II) are those wherein:

25

Y is O;

30

R₁ is C1-5 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl, piperazinyl, pyranyl and thiopyranyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl or amino, wherein R₁ is optionally substituted by one or more R_b;

35

40

45

R_b is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-3 alkoxy, phenoxy, C1-3 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be

independently substituted by C1-5alkyl, phenyl or naphthyl; C1-5
5 alkoxy carbonylamino, C1-5 alkyl carbamoyloxy, aryl carbamoyloxy, C1-5
alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl,
arylamino sulfonyl, amino wherein the nitrogen atom may be independently mono
10 or di-substituted by C1-5alkyl, phenyl, naphthyl, heterocyclyl selected from the
group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl
selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,
thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl,
benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy,
15 oxo, carboxy and cyano, R_b may be further optionally substituted by one or more
R_c;

R_c is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl,
15 aryl, C1-3 alkoxy, phenoxy, halogen, hydroxy, oxo, carboxy and cyano;

15 R₂ is H;

R₃ is C1-5 alkyl, C3-6 cycloalkyl or phenyl, wherein R₃ is optionally substituted by one
20 or more R_d;

20 R_d is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl,
naphthyl, heterocyclyl selected from the group consisting of piperidinyl,
morpholinyl and piperazinyl; heteroaryl selected from the group consisting of
furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, quinolinyl and
25 isoquinolinyl, C1-5 alkoxy, phenoxy, aroyl, C1-5 alkoxy carbonyl,
aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen
atom may be independently mono or di-substituted by C1-5 alkyl, phenyl,
naphthyl, heterocyclyl selected from the group consisting of piperidinyl,
30 morpholinyl and piperazinyl or heteroaryl selected from the group consisting of
furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl,
C1-5 alkanoylamino, aroylamino, C1-3 alkylthio wherein the sulfur atom may be
oxidized to a sulfoxide or sulfone, phenylthio wherein the sulfur atom may be
35 oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be
independently substituted by C1-3 alkyl, phenyl or heteroaryl selected from the group
consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl
and indolyl, C1-5 alkoxy carbonylamino, C1-5 alkyl carbamoyloxy,
arylcaramoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein
40 the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl,
phenyl, heterocyclyl selected from the group consisting of piperidinyl,
morpholinyl and piperazinyl or heteroaryl selected from the group consisting of
furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl,
halogen, hydroxy, oxo, carboxy and cyano, R_d may be further optionally
substituted by one or more R_e;

R_c is selected from the group consisting of C1-5 alkyl, C5-6 cycloalkyl, phenyl, naphthyl, arylC1-3alkyl, C1-5 alkoxy, phenoxy, arylC1-3alkoxy, aroyl, amino, halogen, hydroxy, oxo, carboxy and cyano;

5

R₄ is H;

10 R₆ is H, C1-5 alkyl, C3-6 cycloalkyl, phenyl or cyano, wherein R₆ is optionally substituted by one or more R_f,

15 R_f is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 alkoxy, aryloxy, arylC1-3alkoxy, heteroarylC1-3alkoxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, C1-5 alkanoylamino, aroylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylC1-3alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl or phenyl, C1-5 alkoxycarbonylamino, C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, halogen, hydroxy, oxo, carboxy and cyano, R_f may be further optionally substituted by one or more R_g;

35 R_g is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl optionally substituted by one or more groups selected from halogen or methyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, pyrimidinyl, pyrazinyl and indolyl, C1-5 alkoxy, aryloxy, arylC1-3alkoxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or aryl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom

5 may be independently substituted by C1-5 alkyl or aryl, C1-5 alkoxy carbonylamino, aryloxy carbonylamino, C1-5 alkyl carbamoyloxy, aryl carbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or aryl, halogen, hydroxy, oxo, carboxy and cyano;

10 R_h is selected from the group consisting of C1-5 alkyl, phenyl, C1-5 alkoxy carbonyl, aryloxy carbonyl, aryl C1-3 alkoxycarbonyl, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with C1-5 alkyl, C3-6 cycloalkyl, phenyl, naphthyl or aryl C1-3 alkyl; halogen, hydroxy, carboxy and cyano.

15

Still yet even more preferred compounds of the formula(II) are those wherein:

20 R₁ is C1-3 alkyl, C5-6 cycloalkyl, phenyl, naphthyl, heterocycl selected from the group consisting of piperidinyl, morpholinyl, piperazinyl, pyranyl and thiopyranyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl or amino, wherein R₁ is optionally substituted by one or more R_b;

25

R_b is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl, heterocycl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-3 alkoxy, C1-3 alkoxy carbonyl, aryloxy carbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, phenyl or heteroaryl selected from the group consisting of pyrrolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl and benzthiazolyl C1-5 alkanoylamino, aroylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-3 alkyl or phenyl, C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, phenyl, heterocycl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of pyrrolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy and cyano, R_b may be further optionally substituted by one or more R_c;

R_c is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, C1-3 alkoxy, halogen and hydroxy;

5 R₃ is C1-5 alkyl, C5-6 cycloalkyl or phenyl wherein R₃ is optionally substituted by one or more R_d;

10 R_d is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, 4-piperidinyl, 4-morpholinyl, piperazinyl, furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-5 alkoxy, phenoxy, aroyl, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or phenyl, C1-5 alkanoylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-3 alkyl or phenyl, C1-5 alkoxycarbonylamino, C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, halogen, hydroxy, oxo, carboxy and cyano, R_d may be further optionally substituted by one or more R_e;

20 R_e is selected from the group consisting of C1-5 alkyl, C5-6 cycloalkyl, phenyl, benzyl, C1-5 alkoxy, phenoxy, benzyloxy, aroyl, halogen, hydroxy, oxo, carboxy and cyano;

25 R₅ is H or C1-3alkyl;

30 R₆ is H, C1-5 alkyl, phenyl or cyano, wherein R₆ is optionally substituted by one or more R_f;

35 R_f is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-3 alkoxy, benzyloxy, pyridylC1-3alkoxy, thienylC1-3alkoxy, furanylC1-3alkoxy, C1-3 alkoxycarbonyl, phenoxyoxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, C1-5 alkanoylamino, aroylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl or phenyl, C1-3 alkoxycarbonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or phenyl, halogen, hydroxy, oxo, carboxy and cyano, R_f may be further optionally substituted by one or more R_g;

40 45 R_g is selected from the group consisting of C1-3 alkyl, phenyl optionally substituted by one or more groups selected from the group consisting of halogen and methyl, heterocyclcyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl and pyridinyl, C1-3 alkoxy,

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aryloxy, benzyloxy, C1-5 alkoxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or phenyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl or phenyl, C1-5 alkoxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-3 alkylsulfonylamino, arylsulfonylamino, C1-3 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, halogen, hydroxy, oxo, carboxy and cyano;

10

15

R_h is selected from the group consisting of C1-3 alkyl, phenyl, C1-3 alkoxycarbonyl, phenoxyoxycarbonyl, benzyloxy, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with a group selected from the group consisting of C1-5 alkyl, phenyl and benzyl, halogen, hydroxy, carboxy and cyano.

20

Even more preferred compounds of the formula (II) are those wherein:

25

R_1 is C5-6 cycloalkyl, phenyl, naphthyl, piperidinyl, morpholinyl, piperazinyl, pyranyl, thiopyranyl, furanyl, thienyl, pyrrolyl or amino, wherein R_1 is optionally substituted by one or more R_b ;

30

R_b is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl, furanyl, thienyl, pyrrolyl, imidazolyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, C1-3 alkoxy, C1-3 alkoxycarbonyl, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; C1-5 alkanoylamino, aroylamino, ureido wherein either nitrogen atom may be independently substituted by C1-3 alkyl or phenyl; C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, halogen, hydroxy, oxo, carboxy and cyano, R_b may be further optionally substituted by one or more R_c ;

35

R_c is selected from the group consisting of C1-3 alkyl, C1-3 alkoxy, halogen and hydroxy;

40

R_3 is C1-5 alkyl, C5-6 cycloalkyl or phenyl, wherein R_3 is optionally substituted by one or more groups of the formula R_d ;

45

R_d is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, 4-piperidinyl, furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-3 alkoxy, C1-5 alkoxycarbonyl, C1-5 alkanoyloxy, benzoyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, C1-5

alkanoylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, C1-3 alkoxycarbonylamino, C1-3 alkylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, halogen, hydroxy, oxo, carboxy and cyano, R_d may be further optionally substituted by one or more R_e;

5 R_e is selected from the group consisting of C1-3 alkyl, phenyl, benzyl, C1-3 alkoxy, phenoxy, benzyloxy, benzoyl, halogen, hydroxy, oxo, carboxy and cyano;

10 wherein the configuration at the stereocenter defined by R₂ and R₃ and the carbon they are attached to is defined as L;

R_f is H or methyl;

15 R₆ is C1-5 alkyl, phenyl or cyano wherein R₆ is optionally substituted by one or more groups of the formula R_f;

20 R_f is selected from the group consisting of methyl, C3-6 cycloalkyl, phenyl, naphthyl, furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-3 alkoxy, benzyloxy, pyridylC1-3alkoxy, thienylC1-3alkoxy, furanylC1-3alkoxy, C1-5 alkanoylamino, aroylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, C1-3 alkoxycarbonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or phenyl, halogen, hydroxy, oxo, carboxy and cyano, R_f may be further optionally substituted by one or more R_g;

25 R_g is selected from the group consisting of C1-3 alkyl, phenyl optionally substituted by one or more groups selected from halogen or methyl, C1-3 alkoxy, aryloxy, benzyloxy, C1-3 alkoxycarbonyl, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, C1-5 alkanoylamino, aroylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, halogen, hydroxy, oxo, carboxy and cyano;

30 35 R_h is selected from the group consisting of C1-3 alkyl, phenyl, C1-3 alkoxycarbonyl, benzyloxy and carboxy.

Much more preferred compounds of formula (II) are those wherein:

40

R₁ is cyclohexyl, phenyl, naphthyl, piperidinyl, morpholinyl, piperazinyl, pyranyl, thiopyranyl or amino wherein R₁ is optionally substituted by one or more R_b;

45 R_b is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl, furanyl, thienyl, pyrrolyl, imidazolyl, indolyl, benzofuranyl, benzothienyl,

benzimidazolyl, benzthiazolyl, C1-3 alkoxy, C1-3 alkoxycarbonyl, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, halogen, hydroxy, oxo, carboxy and cyano, R_b may be further optionally substituted by one or more R_c;

10 R_c is selected from the group consisting of C1-3 alkoxy, halogen and hydroxy,

R₃ is C1-5 alkyl or C5-6 cycloalkyl wherein R₃ is optionally substituted by one or more R_d;

15 R_d is selected from the group consisting of methyl, C3-6 cycloalkyl, phenyl, naphthyl, thienyl, imidazolyl, pyridinyl, indolyl, C1-4 alkoxy, C1-5 alkanoylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, halogen, hydroxy, oxo, carboxy and cyano, R_d may be further optionally substituted by one or more R_e;

20 R_e is selected from the group consisting of methyl, phenyl, benzyl, methoxy, phenoxy, benzyloxy, benzoyl, halogen and hydroxy;

25 R₆ is C1-5 alkyl or phenyl, wherein R₆ is optionally substituted by one or more R_f;

30 R_f is selected from the group consisting of C3-6 cycloalkyl, phenyl, naphthyl, thienyl, imidazolyl, pyridinyl, indolyl, methoxy, benzyloxy, C1-3 alkanoylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, methoxycarbonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, halogen, hydroxy, carboxy and cyano, R_f may be further optionally substituted by one or more R_g;

35 R_g is selected from the group consisting of methyl, phenyl optionally substituted by one or more groups selected from halogen or methyl, methoxy, phenoxy, benzyloxy, methoxycarbonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, halogen, hydroxy and carboxy;

40 R_h is selected from the group consisting of vinyl, phenyl, methoxycarbonyl, benzyloxycarbonyl and carboxy;

45

Penultimately preferred compounds of the formula (II) are those wherein:

5 R₁ is cyclohexyl, phenyl, naphthyl, piperidinyl, morpholinyl, piperazinyl, pyranyl or thiopyranyl, wherein R₁ is optionally substituted by one or more R_b;

10 R_b is selected from the group consisting of pyrrolyl, imidazolyl, indolyl, benzimidazolyl, methoxy, methoxycarbonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, halogen, hydroxy and carboxy, R_b may be further optionally substituted by one or more R_c;

R_c is selected from the group consisting of methoxy, halogen and hydroxy;

15 R_d is selected from the group consisting of methyl, C3-6 cycloalkyl, phenyl, naphthyl, C1-4 alkoxy, C1-3 alkanoylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, halogen, hydroxy, oxo, carboxy and cyano, R_d may be further optionally substituted by one or more R_e;

20 R_e is selected from the group consisting of methyl, phenyl, methoxy, halogen and hydroxy;

R_f is H;

25 R_f is selected from the group consisting of C5-6 cycloalkyl, phenyl, naphthyl, thienyl, indolyl, methoxy, benzyloxy, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, methoxycarbonylamino, halogen, hydroxy, carboxy and cyano, R_f may be further optionally substituted by one or more R_g;

30 R_g is selected from the group consisting of methyl, phenyl optionally substituted by halogen, methoxy, phenoxy, benzyloxy, methoxycarbonyl, halogen, hydroxy and carboxy;

35

R_h is vinyl or phenyl.

Ultimately preferred compounds of formula (II) are those wherein:

40

R₁ is phenyl, naphthyl or 4-morpholinyl wherein R₁ is optionally substituted by one or more R_b;

R_b is selected from the group consisting of benzimidazolyl, methoxy and dimethylamino R_b may be further optionally substituted by R_c wherein R_c is a halogen atom;

5

R₃ is C1-5 alkyl wherein R₃ is optionally substituted by one or more R_d;

10 R_d is selected from the group consisting of C3-6 cycloalkyl, phenyl or naphthyl, R_d may be further optionally substituted by one or more R_e;

R_e is selected from the group consisting of methyl and halogen,

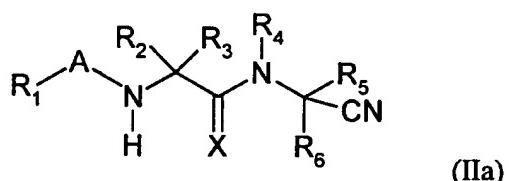
15 R_f is selected from the group consisting of C5-6 cycloalkyl, phenyl, naphthyl, indolyl, benzyloxy, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, halogen and carboxy, R_f may be further optionally substituted by one or more R_g;

20

R_g is selected from the group consisting of methyl, methoxy, methoxycarbonyl, halogen and hydroxy.

25 In another embodiment of the invention, there are provided compounds of the formula (IIa):

30



wherein:

35

A is -C(Y)- or -SO₂-

Y is O, S or NR_a wherein R_a is selected from the group consisting of H, alkyl, aryl, alkoxy, aryloxy, alkylamino and arylamino;

40

R₁ is alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl or amino wherein R₁ is optionally substituted by one or more R_b;

5 R_b is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkoxy, aryloxy, alkanoyl, aroyl, alkoxycarbonyl, aryloxycarbonyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkoxycarbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino; R_b may be further optionally substituted by one or more R_c;

20 R_c is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, arylalkyl, alkoxy, aryloxy, arylalkoxy, alkanoyl, aroyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

25 R₂ is H or alkyl;

R₃ is H, C₂-8alkyl, cycloalkyl, aryl, heterocyclyl or heteroaryl, wherein R₃ is optionally substituted by one or more R_d;

30 R_d is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkoxy, aryloxy, arylalkoxy, alkoxycarbonyl, aryloxycarbonyl, alkanoyl, aroyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkoxycarbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R_d may be further optionally substituted by one or more R_e;

R_e is selected from the group consisting of alkyl, cycloalkyl, aryl, arylalkyl, alkoxy, aryloxy, arylalkoxy, alkanoyl, aroyl, amino, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

5

R₄ is H or alkyl;

10

R₅ is H or alkyl;
R₆ is H, alkyl, cycloalkyl, aryl, heterocyclyl, aryl, heteroaryl or cyano, wherein R₆ is optionally substituted by one or more R_f;

15

R_f is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkoxy, aryloxy, arylalkoxy, alkanoyl, aroyl, alkoxycarbonyl, aryloxycarbonyl, alkanoyloxy, aroyloxy, heteroarylalkoxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkanoylamino, aroylamino, alkylcarbamoyl, arylcarbamoyl, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylalkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkoxycarbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R_f may be further optionally substituted by one or more R_g;

35

R_g is selected from the group consisting of alkyl, cycloalkyl, aryl optionally substituted by one or more groups selected from halogen, methyl or methoxy, heterocyclyl, heteroaryl, alkoxy, aryloxy, arylalkoxy, alkoxycarbonyl, aryloxycarbonyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkanoylamino, aroylamino, alkylcarbamoyl, arylcarbamoyl, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkoxycarbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl,

40

45

aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

- 5 or R₅ and R₆ together with the carbon they are attached form a carbocyclic ring of 3 to 6 carbon atoms, the carbocyclic ring being optionally substituted with one or more R_b;

R_b is selected from the group consisting of alkyl, aryl, alkoxycarbonyl, aryloxycarbonyl, arylalkoxycarbonyl, carbamoyl wherein the nitrogen atom may 10 be optionally mono or di-substituted with a group selected from alkyl, cycloalkyl, aryl, arylalkyl, heterocyclyl, heteroaryl, halogen, hydroxy, carboxy and cyano;

X is O, S or N-OH;

15 and the pharmaceutically acceptable salts, esters or tautomers thereof;

with the following provisos:

20 when Y is O and R₆ is arylalkyl or heteroarylalkyl then R₁ cannot be alkyl, cycloalkyl, aryl, heteroaryl, cycloalkyl-alkyl, aryl-alkyl or aryl-cycloalkyl;

when R₅ is H then R₆ cannot be H;
and

25 when R₁ is C1alkyl then R_b cannot be carbamoyl, alkanoylamino, aroylamino, ureido, alkoxycarbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, amino, amidino or guanidino wherein each said R_b is linked to said R₁ via the nitrogen atom thereof.

30

Preferred compounds of the formula (IIa) are those wherein:

35 Y is O, S or NR_a wherein R_a is H, alkyl or aryl;

40 R₁ is C1-8alkyl, C3-7cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, indolinyl, pyranyl and thiopyranyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl,
45 quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl, phenoazinyl, and amino wherein R₁ is optionally substituted by one or more R_b;

R_b is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, 5
pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl or phenoxyazinyl, C1-8
10 alkoxy, aryloxy, C1-8 alkoxycarbonyl, aryloxycarbonyl, C1-8 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, 15
pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxyazinyl, C1-8 alkanoylamino, aroylamino, 20
C1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, 25
imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, 30
isoquinoliny, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl or phenoxyazinyl, alkoxycarbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, 35
or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, pyrazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, 40
carbazolyl, phenothiazinyl and phenoxyazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino, guanidino; R_b may be further optionally substituted by one or more R_c;

R_c is selected from the group consisting of C1-8 alkyl, C3-6 cycloalkyl, 45
aryl, C1-8 alkoxy, aryloxy, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

R₃ is H, C2-8 alkyl, C3-7 cycloalkyl, aryl wherein R₃ is optionally substituted by one or
5 more R_d;

R_d is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl,
heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl,
morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from
10 the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl,
pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl,
pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl,
benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl,
15 quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoazinyl, C1-8
alkoxy, aryloxy, alkanoyl, aroyl, C1-8 alkoxy carbonyl, aryloxycarbonyl, C1-8
alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be
independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected
from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl,
20 thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group
consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl,
isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl,
pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl,
benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl,
25 quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoazinyl, C1-8
alkanoylamino, aroylamino, C1-8 alkylthio wherein the sulfur atom may be
oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be
oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be
independently substituted by alkyl, aryl, heterocyclyl selected from the group
30 consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl
and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl,
pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl,
oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl,
pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl,
35 benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny,
carbazolyl, phenothiazinyl and phenoazinyl, alkoxy carbonylamino,
aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy,
alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl,
40 amino wherein the nitrogen atom may be independently mono or di-substituted by
alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl,
piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl
selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,
thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl,
tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl,
isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl,
45 quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl

and phenoxazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino, guanidino, R_d may be further optionally substituted by one or more R_e;

5 R_e is selected from the group consisting of C1-8 alkyl, C3-6 cycloalkyl, aryl, arylalkyl, C1-8 alkoxy, aryloxy, arylalkoxy, aroyl, amino, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

10 R₆ is H, C1-8 alkyl, C3-7 cycloalkyl, aryl or cyano, wherein R₆ is optionally substituted by one or more R_f;

15 R_f is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8
20 alkoxy, aryloxy, arylC1-8alkoxy, heteroarylC1-8alkoxy, C1-8 alkoxy carbonyl, aryloxycarbonyl, C1-8 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected
25 from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkanoylamino, aroylamino, C1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylC1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, alkoxy carbonylamino, alkyl carbamoyloxy, aryl carbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl
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selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoxyazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R_f may be further optionally substituted by one or more R_g;

R_g is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl optionally substituted by one or more groups selected from halogen, methyl or methoxy, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoxyazinyl, C1-8 alkoxy, aryloxy, arylC1-8alkoxy, C1-8
20 alkoxycarbonyl, aryloxycarbonyl, C1-8 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoxyazinyl, C1-8 alkanoylamino, aroylamino, C1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoxyazinyl, C1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoxyazinyl, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl,

5 morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thieryl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxyazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino, and guanidino;

10 or R₅ and R₆ together with the carbon they are attached form a carbocyclic ring of 3 to 6 carbon atoms, the carbocyclic ring being optionally substituted with one or more R_h;

15 R_h is selected from the group consisting of C1-8 alkyl, aryl, C1-8 alkoxy carbonyl, aryloxycarbonyl, arylC1-8alkoxycarbonyl, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with a group selected from C1-8 alkyl, C3-7 cycloalkyl, aryl, arylC1-8alkyl, heterocyclcyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thieryl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, 20 oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxyazinyl, halogen, hydroxy, carboxy, and cyano; and

25 X is O or S.

30 More preferred compounds of the formula (IIa) are those wherein:

35 Y is O or S;

R₁ is C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocyclcyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, indolinyl, pyranyl and thiopyranyl, heteroaryl selected from the group consisting of furanyl, thieryl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl or amino; wherein R₁ is optionally substituted by one or more R_b;

45 R_b is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocyclcyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl;, heteroaryl

selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny, C1-5 alkoxy, aryloxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny, C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R_b may be further optionally substituted by one or more R_c;

R_c is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl, aryl, C1-5 alkoxy, aryloxy, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

R₂ is H or C1-3 alkyl;

40 R₃ is H, C2-5 alkyl, C3-7 cycloalkyl, aryl wherein R₃ is optionally substituted by one or more R_d;

45 R_d is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl,

5 triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny, C1-5 alkoxy, aryloxy, C1-5alkanoyl, aroyl, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny, C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R_d may be further optionally substituted by one or more R_e;

35 R_e is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl, aryl, arylalkyl, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, aroyl, amino, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

40 R₄ is H or C1-3 alkyl

45 R₅ is H or C1-8 alkyl

R₆ is H, C1-5 alkyl, C3-7 cycloalkyl, aryl or cyano, wherein R₆ is optionally substituted by one or more R_f;

R_f is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, heteroarylC1-5alkoxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylC1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R_f may be further optionally substituted by one or more R_g;

R_g is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, aryl optionally substituted by one or more groups selected from halogen, methyl or methoxy, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl,

benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalanyl, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, C1-5
5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted
by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and
10 indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and
15 quinoxalanyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl,
20 heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalanyl, C1-5
25 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and
30 indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalanyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and
guanidino;

35 or R₅ and R₆ together with the carbon they are attached form a carbocyclic ring of 3 to 6 carbon atoms, the carbocyclic ring being optionally substituted with one or more R_h;

40 R_h is selected from the group consisting of C1-5 alkyl, aryl, C1-5 alkoxycarbonyl, aryloxycarbonyl, arylC1-5alkoxycarbonyl, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with a group selected from C1-5 alkyl, C3-7 cycloalkyl, aryl, arylC1-5alkyl, heterocyclyl selected from the group
45 consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalanyl, halogen, hydroxy, carboxy and cyano.

5 Even more preferred compounds of the formula (IIa) are those wherein:

Y is O;

10 R₁ is C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocycl selected from the group consisting of piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, pyranyl and thiopyranyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl; or amino wherein R₁ is
15 optionally substituted by one or more R_b;

R_b is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl
20 selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 alkoxy, aryloxy, C1-5 alkoxy carbonyl, aryloxy carbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-
25 substituted by C1-5 alkyl, phenyl, naphthyl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5
30 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl or aryl, C1-5 alkoxy carbonylamino, aryloxy carbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5
35 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy, cyano and nitro, R_b may be further optionally substituted by one or more R_c;
40
45 R_c is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl, aryl, C1-5 alkoxy, aryloxy, halogen, hydroxy, oxo, carboxy and cyano;

R₂ is H or methyl;

5 R₃ is H, C2-5 alkyl, C3-7 cycloalkyl or phenyl wherein R₃ is optionally substituted by one or more R_d;

10 R_d is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 alkoxy, aryloxy, aroyl, C1-5 alkoxy carbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 alkoxy carbonylamino, aryloxycarbonylamino, C1-5 alkyl carbamoyloxy, aryl carbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy and cyano, R_d may be further optionally substituted by one or more R_e.

40 R_e is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl, aryl, arylC1-5alkyl, C1-5 alkoxy, aryloxy, arylC1-3alkoxy, aroyl, amino, halogen, hydroxy, oxo, carboxy and cyano;

45 R₄ is H or methyl;

45 R₅ is H or C1-5 alkyl;

R₆ is H, C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl or cyano, wherein R₆ is optionally substituted by one or more R_f;

5 R_f is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, heteroarylC1-5alkoxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylC1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy and cyano, R_f may be further optionally substituted by one or more R_g;

40 R_g is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, phenyl optionally substituted by one or more groups selected from halogen, methyl or methoxy, naphthyl optionally substituted by one or more groups selected from halogen, methyl or methoxy, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl,

- pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl,
benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny, 5
C1-5 alkoxy, aryloxy, arylC1-5alkoxy, C1-5 alkoxycarbonyl,
aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the
nitrogen atom may be independently mono or di-substituted by C1-5 alkyl,
aryl, heterocycl selected from the group consisting of piperidinyl,
morpholinyl and piperazinyl or heteroaryl selected from the group
consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl,
pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl,
benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino,
10 aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a
sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a
sulfoxide or sulfone, ureido wherein either nitrogen atom may be
independently substituted by C1-5 alkyl, aryl, heterocycl selected from
15 the group consisting of piperidinyl, morpholinyl and piperazinyl or
heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl,
oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl,
benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl,
C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5
20 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino,
arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino
wherein the nitrogen atom may be independently mono or di-substituted
by C1-5 alkyl, aryl, heterocycl selected from the group consisting of
25 pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl or heteroaryl
selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,
thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl,
benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, halogen,
hydroxy, oxo, carboxy and cyano;
- 30 or R₅ and R₆ together with the carbon they are attached form a carbocyclic ring of 3 to 6
carbon atoms, the carbocyclic ring being optionally substituted with one or more R_h;
- R_h is selected from the group consisting of C1-5 alkyl, phenyl, naphthyl, C1-5
35 alkoxycarbonyl, aryloxycarbonyl, arylC1-3alkoxycarbonyl, carbamoyl wherein
the nitrogen atom may be optionally mono or di-substituted with a group selected
from C1-5 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, arylC1-3alkyl, heterocycl
selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and
40 piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl,
pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl,
benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl,
halogen, hydroxy, carboxy and cyano; and

X is O.

Yet even more preferred compounds of the formula (IIa) are those wherein:

5 Y is O;

- R₁ is C1-5 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl, piperazinyl, pyranyl and thiopyranyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl or amino, wherein R₁ is optionally substituted by one or more R_b;
- 10 R_b is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-3 alkoxy, phenoxy, C1-3 alkoxy carbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, phenyl or naphthyl; C1-5 alkoxy carbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy and cyano, R_b may be further optionally substituted by one or more R_c;
- 15 20 25 30 35 40 R_c is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, aryl, C1-3 alkoxy, phenoxy, halogen, hydroxy, oxo, carboxy and cyano;
- 45 R₂ is H;
- R₃ is C2-5 alkyl, C3-6 cycloalkyl or phenyl, wherein R₃ is optionally substituted by one or more R_d;

R_d is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, quinolinyl and isoquinolinyl, C1-5 alkoxy, phenoxy, aroyl, C1-5 alkoxy carbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, C1-5 alkanoylamino, aroylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, phenylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-3 alkyl, phenyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, C1-5 alkoxy carbonylamino, C1-5 alkyl carbamoyloxy, aryl carbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, phenyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, halogen, hydroxy, oxo, carboxy and cyano, R_d may be further optionally substituted by one or more R_e;

R_e is selected from the group consisting of C1-5 alkyl, C5-6 cycloalkyl, phenyl, naphthyl, arylC1-3alkyl, C1-5 alkoxy, phenoxy, arylC1-3alkoxy, aroyl, amino, halogen, hydroxy, oxo, carboxy and cyano;

R_d is H;

R_f is H, C1-5 alkyl, C3-6 cycloalkyl, phenyl or cyano, wherein R_f is optionally substituted by one or more R_f;

R_f is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 alkoxy, aryloxy, arylC1-3alkoxy, heteroarylC1-3alkoxy, C1-5 alkoxy carbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, C1-5 alkanoylamino, aroylamino, C1-3 alkylthio wherein the sulfur atom may be

oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be
5 oxidized to a sulfoxide or sulfone, arylC1-3alkylthio wherein the sulfur atom may
be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be
independently substituted by C1-5 alkyl or phenyl, C1-5 alkoxy carbonylamino,
10 C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom
may be independently mono or di-substituted by C1-5 alkyl, phenyl, naphthyl,
15 heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and
piperazinyl or heteroaryl selected from the group consisting of furanyl, thieryl,
pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, halogen, hydroxy,
20 oxo, carboxy and cyano, R_f may be further optionally substituted by one or more
R_g;

15 R_g is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl,
phenyl optionally substituted by one or more groups selected from halogen
25 or methyl, heterocyclyl selected from the group consisting of pyrrolidinyl,
piperidinyl, morpholinyl and piperazinyl, heteroaryl selected from the
group consisting of furanyl, thieryl, pyrrolyl, oxazolyl, thiazolyl,
30 imidazolyl, pyridinyl, pyrimidinyl, pyrazinyl and indolyl, C1-5 alkoxy,
aryloxy, arylC1-3alkoxy, C1-5 alkoxy carbonyl, aryloxycarbonyl, C1-5
alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be
independently mono or di-substituted by C1-5 alkyl or aryl, C1-5
alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may
be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may
be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom
may be independently substituted by C1-5 alkyl or aryl, C1-5
35 alkoxy carbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy,
arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5
alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom
may be independently mono or di-substituted by C1-5 alkyl or aryl,
40 halogen, hydroxy, oxo, carboxy and cyano;

or R₅ and R₆ together with the carbon they are attached form a carbocyclic ring of 3 to 6
carbon atoms, the carbocyclic ring being optionally substituted with one or more R_h;

35 R_h is selected from the group consisting of C1-5 alkyl, phenyl, C1-5
alkoxy carbonyl, aryloxycarbonyl, arylC1-3alkoxy carbonyl, carbamoyl wherein
the nitrogen atom may be optionally mono or di-substituted with C1-5 alkyl, C3-6
cycloalkyl, phenyl, naphthyl or arylC1-3alkyl; halogen, hydroxy, carboxy and
cyano.

40

Still yet even more preferred compounds of the formula(IIa) are those wherein:

45

R₁ is C1-3 alkyl, C5-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl, piperazinyl, pyranyl and thiopyranyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl or amino, wherein R₁ is optionally substituted by one or more R_b;

5 R_b is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-3 alkoxy, C1-3 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, phenyl or heteroaryl selected from the group consisting of pyrrolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl and benzthiazolyl C1-5 alkanoylamino, aroylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-3alkyl or phenyl, C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3alkyl, phenyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of pyrrolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy and cyano, R_b may be further optionally substituted by one or more R_c;

10 R_c is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, C1-3 alkoxy, halogen and hydroxy;

15 30 R₃ is C2-5 alkyl, C5-6 cycloalkyl or phenyl wherein R₃ is optionally substituted by one or more R_d;

20 R_d is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, 4-piperidinyl, 4-morpholinyl, piperazinyl, furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-5 alkoxy, phenoxy, aroyl, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or phenyl, C1-5 alkanoylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-3 alkyl or phenyl, C1-5 alkylsulfonylamino, C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, halogen, hydroxy, oxo, carboxy and cyano, R_d may be further optionally substituted by one or more R_e;

R_e is selected from the group consisting of C1-5 alkyl, C5-6 cycloalkyl, phenyl, benzyl, C1-5 alkoxy, phenoxy, benzyloxy, aroyl, halogen, hydroxy, oxo, carboxy and cyano;

5 R₅ is H or C1-3alkyl;

R₆ is H, C1-5 alkyl, phenyl or cyano, wherein R₆ is optionally substituted by one or more R_f;

10 R_f is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-3 alkoxy, benzyloxy, pyridylC1-3alkoxy, thienylC1-3alkoxy, furanylC1-3alkoxy, C1-3 alkoxycarbonyl, phenoxyoxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, C1-5 alkanoylamino, aroylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl or phenyl, C1-3 alkoxycarbonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or phenyl, halogen, hydroxy, oxo, carboxy and cyano, R_f may be further optionally substituted by one or more R_g;

25 R_g is selected from the group consisting of C1-3 alkyl, phenyl optionally substituted by one or more groups selected from the group consisting of halogen and methyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl and pyridinyl, C1-3 alkoxy, aryloxy, benzyloxy, C1-5 alkoxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or phenyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl or phenyl, C1-5 alkoxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-3 alkylsulfonylamino, arylsulfonylamino, C1-3 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, halogen, hydroxy, oxo, carboxy and cyano;

30 or R₅ and R₆ together with the carbon they are attached form a carbocyclic ring of 3 to 5 carbon atoms, the carbocyclic ring being optionally substituted with one or more R_h;

40 R_h is selected from the group consisting of C1-3 alkyl, phenyl, C1-3 alkoxycarbonyl, phenoxyoxycarbonyl, benzyloxy, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with a group selected from the group consisting of C1-5 alkyl, phenyl and benzyl, halogen, hydroxy, carboxy and cyano.

- 5 Even more preferred compounds of the formula (IIa) are those wherein:
- 10 R₁ is C5-6 cycloalkyl, phenyl, naphthyl, piperidinyl, morpholinyl, piperazinyl, pyranyl, thiopyranyl, furanyl, thienyl, pyrrolyl or amino, wherein R₁ is optionally substituted by one or more R_b;
- 15 R_b is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl, furanyl, thienyl, pyrrolyl, imidazolyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, C1-3 alkoxy, C1-3 alkoxycarbonyl, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; C1-5 alkanoylamino, aroylamino, ureido wherein either nitrogen atom may be independently substituted by C1-3alkyl or phenyl;, C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3alkyl or phenyl, halogen, hydroxy, oxo, carboxy and cyano, R_b may be further optionally substituted by one or more R_c;
- 20 R_c is selected from the group consisting of C1-3alkyl, C1-3alkoxy, halogen and hydroxy;
- 25 R₃ is C2-5 alkyl, C5-6 cycloalkyl or phenyl, wherein R₃ is optionally substituted by one or more groups of the formula R_d;
- 30 R_d is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, 4-piperidinyl, furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-3 alkoxy, C1-5 alkoxycarbonyl, C1-5 alkanoyloxy, benzyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, C1-5 alkanoylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, C1-3 alkoxycarbonylamino, C1-3 alkylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, halogen, hydroxy, oxo, carboxy and cyano, R_d may be further optionally substituted by one or more R_e;
- 35 R_e is selected from the group consisting of C1-3 alkyl, phenyl, benzyl, C1-3 alkoxy, phenoxy, benzyloxy, benzoyl, halogen, hydroxy, oxo, carboxy and cyano;
- 40 wherein the configuration at the stereocenter defined by R₂ and R₃ and the carbon they are attached to is defined as L;
- R₅ is H or methyl;
- 45 R₆ is C1-5 alkyl, phenyl or cyano wherein R₆ is optionally substituted by one or more groups of the formula R_f;

5 R_f is selected from the group consisting of methyl, C3-6 cycloalkyl, phenyl, naphthyl, furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-3 alkoxy, benzyloxy, pyridylC1-3alkoxy, thienylC1-3alkoxy, furanylC1-3alkoxy, C1-5 alkanoylamino, aroylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, C1-3 alkoxy carbonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or phenyl, halogen, hydroxy, oxo, carboxy and cyano, R_f may be further optionally substituted by one or more R_g;

10

R_g is selected from the group consisting of C1-3 alkyl, phenyl optionally substituted by one or more groups selected from halogen or methyl, C1-3 alkoxy, aryloxy, benzyloxy, C1-3 alkoxy carbonyl, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, C1-5 alkanoylamino, aroylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, halogen, hydroxy, oxo, carboxy and cyano;

15

or R₅ and R₆ together with the carbon they are attached form a carbocyclic ring of 3 to 5 carbon atoms, the carbocyclic ring being optionally substituted with one or more R_h;

20

R_h is selected from the group consisting of C1-3 alkyl, phenyl, C1-3 alkoxy carbonyl, benzyloxy and carboxy.

25

Much more preferred compounds of formula (IIa) are those wherein:

30

R₁ is cyclohexyl, phenyl, naphthyl, piperidinyl, morpholinyl, piperazinyl, pyranyl, thiopyranyl or amino wherein R₁ is optionally substituted by one or more R_b;

35

R_b is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl, furanyl, thienyl, pyrrolyl, imidazolyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, C1-3 alkoxy, C1-3 alkoxy carbonyl, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, halogen, hydroxy, oxo, carboxy and cyano, R_b may be further optionally substituted by one or more R_c;

40

R_c is selected from the group consisting of C1-3 alkoxy, halogen and hydroxy,

45

R₃ is C2-5 alkyl or C5-6 cycloalkyl wherein R₃ is optionally substituted by one or more R_d;

5 R_d is selected from the group consisting of methyl, C3-6 cycloalkyl, phenyl, naphthyl, thienyl, imidazolyl, pyridinyl, indolyl, C1-4 alkoxy, C1-5 alkanoylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, halogen, hydroxy, oxo, carboxy and cyano, R_d may be further optionally substituted by one or more R_e;

10 R_e is selected from the group consisting of methyl, phenyl, benzyl, methoxy, phenoxy, benzyloxy, benzoyl, halogen and hydroxy;

15 R₆ is C1-5 alkyl or phenyl, wherein R₆ is optionally substituted by one or more R_f;

20 15 R_f is selected from the group consisting of C3-6 cycloalkyl, phenyl, naphthyl, thienyl, imidazolyl, pyridinyl, indolyl, methoxy, benzyloxy, C1-3 alkanoylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, methoxycarbonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, halogen, hydroxy, carboxy and cyano, R_f may be further optionally substituted by one or more R_g;

25 25 R_g is selected from the group consisting of methyl, phenyl optionally substituted by one or more groups selected from halogen or methyl, methoxy, phenoxy, benzyloxy, methoxycarbonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, halogen, hydroxy and carboxy;

30 30 or R₅ and R₆ together with the carbon they are attached form a carbocyclic ring of 3 to 5 carbon atoms, the carbocyclic ring being optionally substituted with one or more R_h;

35 R_h is selected from the group consisting of vinyl, phenyl, methoxycarbonyl, benzyloxycarbonyl and carboxy;

40 40 Penultimately preferred compounds of the formula (IIa) are those wherein:

45 R₁ is cyclohexyl, phenyl, naphthyl, piperidinyl, morpholinyl, piperazinyl, pyranyl or thiopyranyl, wherein R₁ is optionally substituted by one or more R_b;

45 R_b is selected from the group consisting of pyrrolyl, imidazolyl, indolyl, benzimidazolyl, methoxy, methoxycarbonyl, amino wherein the nitrogen atom

may be independently mono or di-substituted by C1-3 alkyl, halogen, hydroxy and carboxy, R_b may be further optionally substituted by one or more R_c;

R_c is selected from the group consisting of methoxy, halogen and hydroxy;

5

R_d is selected from the group consisting of methyl, C3-6 cycloalkyl, phenyl, naphthyl, C1-4 alkoxy, C1-3 alkanoylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, halogen, hydroxy, oxo, carboxy and cyano, R_d may be further optionally substituted by one or more R_e;

10

R_e is selected from the group consisting of methyl, phenyl, methoxy, halogen and hydroxy;

R_f is H;

15

R_f is selected from the group consisting of C5-6 cycloalkyl, phenyl, naphthyl, thienyl, indolyl, methoxy, benzyloxy, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, methoxycarbonylamino, halogen, hydroxy, carboxy and cyano, R_f may be further optionally substituted by one or more R_g;

20

R_g is selected from the group consisting of methyl, phenyl optionally substituted by halogen, methoxy, phenoxy, benzyloxy, methoxycarbonyl, halogen, hydroxy and carboxy;

25

or R₅ and R₆ together with the carbon they are attached form a carbocyclic ring of 3 carbon atoms, the carbocyclic ring being optionally substituted with one or more R_h;

30

R_h is vinyl or phenyl.

Ultimately preferred compounds of formula (IIa) are those wherein:

35

R₁ is phenyl, naphthyl or 4-morpholinyl wherein R₁ is optionally substituted by one or more R_b;

40

R_b is selected from the group consisting of benzimidazolyl, methoxy and dimethylamino R_b may be further optionally substituted by R_c wherein R_c is a halogen atom;

45

R₃ is C2-5 alkyl wherein R₃ is optionally substituted by one or more R_d;

R_d is selected from the group consisting of C3-6 cycloalkyl, phenyl or naphthyl,
R_d may be further optionally substituted by one or more R_e;

5 R_e is selected from the group consisting of methyl and halogen,

10 R_f is selected from the group consisting of C5-6 cycloalkyl, phenyl, naphthyl,
indolyl, benzyloxy, methylthio wherein the sulfur atom may be oxidized to a
sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidized to a
sulfoxide or sulfone, halogen and carboxy, R_f may be further optionally
substituted by one or more R_g;

15 R_g is selected from the group consisting of methyl, methoxy, methoxycarbonyl, halogen
and hydroxy and

20 R₅ and R₆ together with the carbon they are attached form a carbocyclic ring of 3 carbon
atoms, the carbocyclic ring being optionally substituted with one or more R_h.

25

The following are representative compounds according to the invention:

30

N-(4-morpholinecarbonyl)-L-leucine (1S-cyano-3-phenylpropyl)amide;

N-(4-morpholinecarbonyl)-L-Homophenylalanine(1S-cyano-3-phenylpropyl)amide;

35

N-(5-dimethylaminonaphth-1-ylsulfonyl)-L-leucine (1S-cyano-3-phenylpropyl)amide;

N-(4-morpholinecarbonyl)-L-leucine-(1S-cyano-3-phenylpropyl)-N-methylamide;

40

N-(4-Morpholinecarbonyl)-L-leucine-[1R,S(benzthiazol-2-ylcarbonyl)-3-phenylpropyl]amide;

N-[(4-Morpholinecarbonyl]-L-leucine-[1R,S-(thiazol-2-ylcarbonyl)-3-phenylpropyl]amide;

45

N-(4-Morpholinecarbonyl)-L-leucine-[1R,S-[(1-(3-N-Benzyl)imidazol-2-ylcarbonyl]-3-phenylpropyl]amide;

50

N-(4-Morpholinecarbonyl)-L-leucine-[1R,S-(2-imidazolylcarbonyl)-3-phenylpropyl]amide;

N- (4-morpholinecarbonyl)-L-leucine (cyanomethyl)amide;

- N-(4-Morpholinecarbonyl)-L-leucine [1*S*-cyano-5-((benzyloxycarbonyl)-amino)-pentyl]amide;
- 5 *N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-3-phenylpropyl)amide;
- N-(4-Morpholinecarbonyl]-L-leucine-(1*S*-cyano-5-aminopentyl)amide;
- N-(4-morpholinecarbonyl]-L-phenylalanine-(1*S*-cyano-3-phenylpropyl)amide;
- 10 *N*-(4-morpholinecarbonyl)-L-(*p*-ethoxy)phenylalanine-(1*S*-cyano-3-phenylpropyl)amide;
- N-(4-Morpholinecarbonyl)-L-leucine-[1*S*-cyano-4-(benzyloxycarbonylamino)-butyl]amide;
- 15 *N*-(4-Morpholinecarbonyl)-L-leucine-[1-(benzthiazol-2-ylcarbonyl)-5-[(benzyloxycarbonyl)amino]-pentyl]amide;
- N*-(1-naphthylsulfonyl)-L-leucine (1*S*-cyano-3-phenylpropyl)amide;
- N*-(4-morpholinecarbonyl)-L-(4-methyl)leucine (1*S*-cyano-3-phenylpropyl)amide;
- 20 *N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-benzyloxyethyl)amide;
- N*-(methanesulfonyl)-D-(*O*-benzyl)serine (1*S*-cyano-3-phenylpropyl)amide;
- N*-(5-dimethylaminonaphth-1-ylsulfonyl)-D-leucine (1*R*-cyano-3-phenylpropyl)amide;
- N*-(4-morpholinecarbonyl)-L-(4-methyl)leucine (1*R*-cyano-2-benzyloxyethyl)amide;
- N*-((4-dimethylaminophenyl)sulfonyl)-L-leucine (1*S*-cyano-3-(phenylpropyl))amide;
- 25 *N*-(t-Butoxycarbonyl)-L-leucine [1-(Benzothiazo-2-ylcarbonyl)-3-phenylpropyl]amide;
- N*-(5-dimethylaminonaphth-1-ylsulfonyl)-L-leucine [1-(Benzothiazol-2-ylcarbonyl)-3-phenylpropyl]amide;
- 30 *N*-(4-methoxy-phenylsulfonyl)-L-leucine [1-(Benzothiazol-2-ylcarbonyl)-3-phenylpropyl]amide;
- N*-(4-Morpholinecarbonyl)-L-leucine-[1*R,S*(benzoxazol-2-ylcarbonyl)-3-phenylpropyl]amide;
- 35 *N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2*R*-benzyloxypropyl)amide;
- N*-(4-Morpholinecarbonyl)-L-leucine-[1*R,S*-[(4-phenylthiazol-2-yl)-carbonyl]-3-phenylpropyl]amide;
- 40 *N*-(4-morpholinecarbonyl)-D-leucine (1*S*-cyano-3-phenylpropyl)amide;

- N*-(4-morpholinecarbonyl)-L-leucine [[1-[(6-phenylcarbamoyl)benzothiazol-2-ylcarbonyl]-3-phenylpropyl]]amide;
- 5 *N*-(methylsulfonyl)-L-leucine [1-(Benzothiazol-2-ylcarbonyl)-3-phenylpropyl]amide;
- N*-(4-morpholinecarbonyl)-L-(p-phenyl)phenylalanine (1*S*-cyano-3-phenylpropyl)amide;
- 10 *N*-(4-Morpholinecarbonyl)-L-leucine-[1*R,S*-[(5-phenylthiazol-2-yl)-carbonyl]-3-phenylpropyl]amide;
- 10 *N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(benzylsulfanyl)ethyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(2-chlorophenyl)methyloxyethyl)amide;
- 15 *N*-(4-morpholinecarbonyl)-L-phenylglycine (1*S*-cyano-3-phenylpropyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine [1-(Benzothiazol-2-ylcarbonyl)-2-benzyloxyethyl]amide;
- 20 *N*-(4-Morpholinecarbonyl)-L-leucine-[[6-(carbomethoxy)-benzoxazol-2-ylcarbonyl]-3-phenylpropyl]amide;
- N*-(5-dimethylaminonaphth-1-ylsulfonyl)-L-(4-methyl)leucine (1*R*-cyano-2-benzyloxyethyl)amide;
- 25 *N*-(4-morpholinecarbonyl)-L-cyclohexylalanine (1*S*-cyano-3-phenylpropyl)amide;
- N*-(4-Morpholinecarbonyl)-L-leucine-[1*R,S*-[(4-(4-benzyloxycarbonylamino)phenylthiazol-2-yl)-carbonyl]-3-phenylpropyl]amide;
- 30 *N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(3-methoxyphenyl)methyloxyethyl)amide;
- N*-(4-morpholinecarbonyl)-L-(4-methyl)leucine (1*R*-cyano-2-(benzylsulfanyl)ethyl)amide;
- 35 *N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(benzylsulfonyl)ethyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(benzylsulfinyl)ethyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-((4-methoxyphenyl)methylsulfanyl)ethyl)amide;
- 40 *N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-((4-methylphenyl)methylsulfanyl)ethyl)amide;

- N*-(4-morpholinecarbonyl)-L-leucine (*1R*-cyano-2-(4-chlorophenyl)methyloxyethyl)amide;
- 5 *N*-(4-morpholinecarbonyl)-L-leucine (*1R*-cyano-2-(3-chlorophenyl)methyloxyethyl)amide;
- N*-(5-dimethylaminonaphth-1-ylsulfonyl)-L-leucine (*1R*-cyano-2-benzyloxyethyl)amide;
- 10 *N*-(4-Morpholinecarbonyl]-L-leucine *1S*-(2-phenyloxazol-5-yl)carbonyl)-3-phenylpropylamide;
- 15 *N*-(4-morpholinecarbonyl)-L-(*p*-phenylcarbonyl)phenylalanine (*1S*-cyano-3-phenylpropyl)amide;
- 20 *N*-(4-morpholinecarbonyl)-L-leucine (*1R*-cyano-2-(2-methylphenyl)methyloxyethyl)amide;
- 25 *N*-(4-morpholinecarbonyl)-L-leucine (*1R*-cyano-2-(3-methylphenyl)methyloxyethyl)amide;
- 30 *N*-(4-morpholinecarbonyl)-L-leucine (*1R*-cyano-2-(4-methylphenyl)methyloxyethyl)amide;
- N*-(4-Morpholinecarbonyl]-L-leucine *1RS*-(5-phenyloxazol-2-yl)carbonyl)-3-phenylpropylamide;
- 35 *N*-(4-morpholinecarbonyl)-L-cyclohexylalanine (*1R*-cyano-2-benzyloxyethyl)amide;
- 40 *N*-(4-morpholinecarbonyl)-L-nor-leucine (*1S*-cyano-3-phenylpropyl)amide;
- N*-(Benzylloxycarbonyl)-L-(O-t-butyl)serine (*1R*-cyano-2-benzyloxyethyl)amide;
- 45 *N*-(4-Morpholinecarbonyl]-L-leucine *1S*-(oxazol-2-ylcarbonyl)-3-phenylpropylamide;
- 50 *N*-(4-morpholinecarbonyl)-L-(4-methyl)leucine [1-(Benzothiazol-2-ylcarbonyl)-3-phenylpropyl]amide;
- 55 *N*-(5-dimethylaminonaphth-1-ylsulfonyl)-L-cyclohexylalanine (*1R*-cyano-2-benzyloxyethyl)amide;
- 60 *N*-(4-morpholinecarbonyl)-L-leucine (*1R*-cyano-2-(3-carbomethoxyphenyl)methyloxyethyl)amide;
- 65 *N*-(4-morpholinecarbonyl)-L-leucine (*1R*-cyano-2-(4-carbomethoxyphenyl)methyloxyethyl)amide;

N-(4-Morpholinecarbonyl)-L-leucine 1*S*-(pyrid-2-ylcarbonyl)-3-phenylpropylamide;

5 *N*-(4-Morpholinecarbonyl)-L-leucine-[1*R*,*S*-[(4-(2-benzyloxyamino)phenyl-thiazol-2-yl)-carbonyl]-3-phenylpropyl]amide;

10 *N*-(4-morpholinecarbonyl)-L-(O-t-butyl)serine (1*R*-cyano-2-benzyloxyethyl)amide;

15 *N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-hydroxyethyl)amide;

20 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-3-(carbo-*t*-butoxy)propyl)amide;

25 *N*-(cyclohexylcarbonyl)-L-leucine (1*R*-cyano-2-benzyloxyethyl)amide;

30 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-3-(carbo-*t*-butoxy)ethyl)amide;

35 *N*-(4-morpholinecarbonyl)-L-leucine dicyanomethylamide;

40 *N*-(4-morpholinecarbonyl)-L-(2-naphthyl)alanine (1*S*-cyano-3-phenylpropyl)amide;

45 *N*-(4-morpholinecarbonyl)-L-(O-Benzyl)glutamate (1*S*-cyano-3-phenylpropyl)amide;

50 *N*-(4-morpholinecarbonyl)-L-homo-tyrosine (1*S*-cyano-3-phenylpropyl)amide;

55 *N*-(4-morpholinecarbonyl)-L-norvaline (1*S*-cyano-3-phenylpropyl)amide;

60 *N*-(4-morpholinecarbonyl)-L-(2-chlorophenyl)alanine (1*S*-cyano-3-phenylpropyl)amide;

65 *N*-Benzoyl-L-leucine (1*R*-cyano-2-benzyloxyethyl)amide;

70 *N*-(4-morpholinecarbonyl)-L-(4,5-dehydro)leucine(1*S*-cyano-3-phenylpropyl)amide;

75 *N*-(4-morpholinecarbonyl)-L-(O-methyl)tyrosine(1*S*-cyano-3-phenylpropyl)amide;

80 *N*-(4-morpholinecarbonyl)-L-iso-leucine (1*S*-cyano-3-phenylpropyl)amide;

85 *N*-(4-morpholinecarbonyl)-L-(4-nitrophenyl)alanine (1*S*-cyano-3-phenylpropyl)amide;

90 *N*-(4-morpholinecarbonyl)-L-(4-fluorophenyl)alanine (1*S*-cyano-3-phenylpropyl)amide;

95 *N*-(4-morpholinecarbonyl)-L-tyrosine (1*S*-cyano-3-phenylpropyl)amide;

100 *N*-(4-morpholinecarbonyl)-L-(1-naphthyl)alanine (1*S*-cyano-3-phenylpropyl)amide;

105 *N*-(4-morpholinecarbonyl)-L-methionine (1*S*-cyano-3-phenylpropyl)amide;

110 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(1-benzyl-4-imidazolyl)ethyl)amide;

115 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(1-benzyl-4-imidazolyl)ethyl)amide;

- 5 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(carbobenzyloxy)ethyl)amide;
- 10 *N*-(4-morpholinecarbonyl)-L-leucine(1*S*-cyano-2-(carbobenzyloxy)ethyl)amide;
- 15 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-1-phenylmethyl)amide;
- 20 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-1-phenylmethyl)amide;
- 25 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1-cyanocyclopropyl)amide;
- 30 *N*-(4-morpholinecarbonyl)-L-leucine (1-cyanocyclopropyl)amide;
- 35 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(4-phenylphenyl)ethyl)amide;
- 40 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(4-phenylphenyl)ethyl)amide;
- 45 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(4-benzoylphenyl)ethyl)amide;
- 50 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(4-benzoylphenyl)ethyl)amide;
- 55 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(1-naphthyl)ethyl)amide;
- 60 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(1-naphthyl)ethyl)amide;
- 65 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(2-naphthyl)ethyl)amide;
- 70 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(2-naphthyl)ethyl)amide;
- 75 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(2-chlorophenyl)ethyl)amide;
- 80 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(2-chlorophenyl)ethyl)amide;
- 85 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(4-chlorophenyl)ethyl)amide;
- 90 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(4-chlorophenyl)ethyl)amide;
- 95 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(3,4-dichlorophenyl)ethyl)amide;
- 100 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(3,4-dichlorophenyl)ethyl)amide;
- 105 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyanobut-3-ynyl)amide;

- N*-(4-morpholinecarbonyl)-L-leucine(1*S*-cyanobut-3-ynyl)amide;
- 5 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyanopropyl)amide;
- N*-(4-morpholinecarbonyl)-L-phenylalanine;
- 10 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(4-(2,6-dichloromethoxy)phenyl)ethyl)amide;
- 15 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2*S*-methylbutyl)amide;
- 20 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyanopentyl)amide;
- 25 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2,2-dimethylpropyl)amide;
- 30 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2,2-dimethylpropyl)amide;
- 35 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-3-methylbutyl)amide;
- 40 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(4-nitrophenylethyl)amide;
- 45 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(4-nitrophenylethyl)amide;
- N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyanobutyl)amide;
- N*-(4-morpholinecarbonyl)-L-phenylalanine (1*R*-cyano-2*R*-benzyloxypropyl)amide;
- N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyanoethyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyanoethyl)amide;
- N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-3-(carbobenzyloxy)propyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-3-(carbobenzyloxy)propyl)amide;
- N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(3-benzimidazolyl)ethyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(3-benzimidazolyl)ethyl)amide;

- N*-(4-morpholinecarbonyl)-L-phenylalanine (1-cyano-1-methylethyl)amide;
N-(4-morpholinecarbonyl)-L-leucine (1-cyano-1-methylethyl)amide;
- 5 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(4-hydroxyphenyl)ethyl)amide;
N-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(4-hydroxyphenyl)ethyl)amide;
- 10 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S,3*-dicyanopropyl)amide;
N-(4-morpholinecarbonyl)-L-leucine (1*S,3*-dicyanopropyl)amide;
- 15 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(4-hydroxy-3-iodophenyl)ethyl)amide;
N-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(4-hydroxy-3-iodophenyl)ethyl)amide;
- 20 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S,2*-dicyanoethyl)amide;
N-(4-morpholinecarbonyl)-L-leucine (1*S,2*-dicyanoethyl)amide;
- 25 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*R*-cyano-2-benzyloxyethyl)amide;
N-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(2-thienyl)ethyl)amide;
- 30 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(2-thienyl)ethyl)amide;
N-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-3-(methylsulfonyl)propyl)amide;
- 35 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-3-(methylsulfonyl)propyl)amide;
N-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-phenylethyl)amide;
- 40 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-phenylethyl)amide;
N-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-3-(4-hydroxyphenyl)propyl)amide;
- 45 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-3-(4-hydroxyphenyl)propyl)amide;
N-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-cyclohexylethyl)amide;
N-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-cyclohexylethyl)amide;
N-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(3-chlorophenyl)ethyl)amide;
and
N-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(3-chlorophenyl)ethyl)amide.

Preferred compounds of the invention include:

- 5 *N*-(5-dimethylaminonaphth-1-ylsulfonyl)-L-leucine (1*S*-cyano-3-phenylpropyl)amide;
 N-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-3-phenylpropyl)amide;
 N-(1-naphthylsulfonyl)-L-leucine (1*S*-cyano-3-phenylpropyl)amide;
 N-(4-morpholinecarbonyl)-L-(4-methyl)leucine (1*S*-cyano-3-phenylpropyl)amide;
10 *N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-benzyloxyethyl)amide;
 N-(4-morpholinecarbonyl)-L-(4-methyl)leucine (1*R*-cyano-2-benzyloxyethyl)amide;
 N((4-dimethylaminophenyl)sulfonyl)-L-leucine (1*S*-cyano-3-(phenylpropyl))amide;
 N-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2*R*-benzyloxypropyl)amide;
15 *N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(benzylsulfanyl)ethyl)amide;
 N-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(2-chlorophenyl)methyloxyethyl)amide;
20 *N*-(5-dimethylaminonaphth-1-ylsulfonyl)-L-(4-methyl)leucine (1*R*-cyano-2-benzyloxyethyl)amide;
 N-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(3-methoxyphenyl)methyloxyethyl)amide;
25 *N*-(4-morpholinecarbonyl)-L-(4-methyl)leucine (1*R*-cyano-2-(benzylsulfanyl)ethyl)amide;
 N-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(benzylsulfinyl)ethyl)amide;
30 *N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-((4-methoxyphenyl)methylsulfanyl)ethyl)amide;
 N-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-((4-methylphenyl)methylsulfanyl)ethyl)amide;
35 *N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(4-chlorophenyl)methyloxyethyl)amide;
 N-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(3-chlorophenyl)methyloxyethyl)amide;

- N*-(5-dimethylaminonaphth-1-ylsulfonyl)-L-leucine (*1R*-cyano-2-benzyloxyethyl)amide;
N-(4-morpholinecarbonyl)-L-leucine (*1R*-cyano-2-(2-methylphenyl)methyloxyethyl)amide;
- 5 *N*-(4-morpholinecarbonyl)-L-leucine (*1R*-cyano-2-(3-methylphenyl)methyloxyethyl)amide;
N-(4-morpholinecarbonyl)-L-leucine (*1R*-cyano-2-(4-methylphenyl)methyloxyethyl)amide;
- 10 *N*-(5-dimethylaminonaphth-1-ylsulfonyl)-L-cyclohexylalanine (*1R*-cyano-2-benzyloxyethyl)amide;
- 15 *N*-(4-morpholinecarbonyl)-L-leucine (*1R*-cyano-2-(3-carbomethoxyphenyl)methyloxyethyl)amide;
N-(4-morpholinecarbonyl)-L-leucine (*1R*-cyano-2-(4-carbomethoxyphenyl)methyloxyethyl)amide;
- 20 *N*-(4-morpholinecarbonyl)-L-leucine (*1R*-cyano-2-hydroxyethyl)amide;
N-(4-morpholinecarbonyl)-L-leucine (*1S*-cyano-3-(carbo-*t*-butoxy)propyl)amide;
N-(cyclohexylcarbonyl)-L-leucine (*1R*-cyano-2-benzyloxyethyl)amide;
N-(4-morpholinecarbonyl)-L-leucine (*1S*-cyano-3-(carbo-*t*-butoxy)ethyl)amide;
- 25 *N*-(4-morpholinecarbonyl)-L-leucine (*1S*-cyano-3-phenylpropyl)amide;
N-(4-morpholinecarbonyl)-L-Homophenylalanine(*1S*-cyano-3-phenylpropyl)amide;
N-(4-morpholinecarbonyl)-L-leucine (cyanomethyl)amide;
- 30 *N*-(4-Morpholinecarbonyl)-L-leucine [*1S*-cyano-5-((benzyloxycarbonyl)-amino)-pentyl]amide;
N-(4-Morpholinecarbonyl]-L-leucine-(*1S*-cyano-5-aminopentyl)amide;
- 35 *N*-(4-morpholinecarbonyl]-L-phenylalanine-(*1S*-cyano-3-phenylpropyl)amide;
N-(4-morpholinecarbonyl)-L-(*p*-ethoxy)phenylalanine-(*1S*-cyano-3-phenylpropyl)amide;
- 40 *N*-(4-Morpholinecarbonyl)-L-leucine-[*1S*-cyano-4-(benzyloxycarbonylamino)-butyl]amide;
N-(4-Morpholinecarbonyl)-L-leucine-[*1R,S*(benzthiazol-2-ylcarbonyl)-3-phenylpropyl]amide;

N-(4-Morpholinecarbonyl)-L-leucine-[1R,S(benzoxazol-2-ylcarbonyl)-3-phenylpropyl]amide;

5 N-(4-Morpholinecarbonyl)-L-leucine-[1-(benzthiazol-2-ylcarbonyl)-5-[(benzyloxycarbonyl)amino]-pentyl]amide;

N-(4-Morpholinecarbonyl)-L-leucine-[[6-(carbomethoxy)-benzoxazol-2-ylcarbonyl]-3-phenylpropyl]amide;

10 *N*-(4-morpholinecarbonyl)-L-leucine [[1-[(6-phenylcarbamoyl)benzothiazol-2-ylcarbonyl]-3-phenylpropyl]]amide;

15 *N*-(4-morpholinecarbonyl)-L-(p-phenyl)phenylalanine (1*S*-cyano-3-phenylpropyl)amide;

N-(4-morpholinecarbonyl)-L-phenylglycine (1*S*-cyano-3-phenylpropyl)amide;

N-(4-morpholinecarbonyl)-L-cyclohexylalanine (1*S*-cyano-3-phenylpropyl)amide;

20 *N*-(4-Morpholinecarbonyl)-L-leucine 1*S*-((2-phenyloxazol-5-yl)carbonyl)-3-phenylpropylamide;

N-(4-morpholinecarbonyl)-L-(p-phenylcarbonyl)phenylalanine (1*S*-cyano-3-phenylpropyl)amide;

25 *N*-(4-Morpholinecarbonyl)-L-leucine 1*RS*-((5-phenyloxazol-2-yl)carbonyl)-3-phenylpropylamide;

N-(4-Morpholinecarbonyl)-L-leucine 1*S*-(oxazol-2-ylcarbonyl)-3-phenylpropylamide;

30 *N*-(4-morpholinecarbonyl)-L-cyclohexylalanine (1*R*-cyano-2-benzyloxyethyl)amide;

N-(4-morpholinecarbonyl)-L-nor-leucine (1*S*-cyano-3-phenylpropyl)amide;

35 *N*-(4-morpholinecarbonyl)-L-(4-methyl)leucine [1-(Benzothiazol-2-ylcarbonyl)-3-phenylpropyl]amide;

N-(4-Morpholinecarbonyl)-L-leucine 1*S*-(pyrid-2-ylcarbonyl)-3-phenylpropylamide;

40 *N*-(4-morpholinecarbonyl)-L-(O-t-butyl)serine (1*R*-cyano-2-benzyloxyethyl)amide;

N-(4-morpholinecarbonyl)-L-(2-naphthyl)alanine (1*S*-cyano-3-phenylpropyl)amide;

N-(4-morpholinecarbonyl)-L-(O-Benzyl)glutamate (1*S*-cyano-3-phenylpropyl)amide;

45 *N*-(4-morpholinecarbonyl)-L-homo-tyrosine (1*S*-cyano-3-phenylpropyl)amide;

- N*-(4-morpholinecarbonyl)-L-norvaline (1*S*-cyano-3-phenylpropyl)amide;
- 5 *N*-(4-morpholinecarbonyl)-L-(2-chlorophenyl)alanine (1*S*-cyano-3-phenylpropyl)amide;
- N*-Benzoyl-L-leucine (1*R*-cyano-2-benzyloxyethyl)amide;
- 10 *N*-(4-morpholinecarbonyl)-L-(4,5-dehydro)leucine(1*S*-cyano-3-phenylpropyl)amide;
- 15 *N*-(4-morpholinecarbonyl)-L-(O-methyl)tyrosine(1*S*-cyano-3-phenylpropyl)amide;
- N*-(4-morpholinecarbonyl)-L-iso-leucine (1*S*-cyano-3-phenylpropyl)amide;
- 20 *N*-(4-morpholinecarbonyl)-L-(4-nitrophenyl)alanine (1*S*-cyano-3-phenylpropyl)amide;
- 25 *N*-(4-morpholinecarbonyl)-L-(4-fluorophenyl)alanine (1*S*-cyano-3-phenylpropyl)amide;
- N*-(4-morpholinecarbonyl)-L-tyrosine (1*S*-cyano-3-phenylpropyl)amide;
- 30 *N*-(4-morpholinecarbonyl)-L-(1-naphthyl)alanine (1*S*-cyano-3-phenylpropyl)amide;
- N*-(4-morpholinecarbonyl)-L-methionine (1*S*-cyano-3-phenylpropyl)amide;
- 35 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(1-benzyl-4-imidazolyl)ethyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(1-benzyl-4-imidazolyl)ethyl)amide;
- N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(carbobenzyloxy)ethyl)amide;
- 40 *N*-(4-morpholinecarbonyl)-L-leucine(1*S*-cyano-2-(carbobenzyloxy)ethyl)amide;
- N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-1-phenylmethyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-1-phenylmethyl)amide;
- 45 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(4-benzyloxyphenyl)ethyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(4-benzyloxyphenyl)ethyl)amide;
- N*-(4-morpholinecarbonyl)-L-phenylalanine (1-cyanocyclopropyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1-cyanocyclopropyl)amide;
- N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(4-phenylphenyl)ethyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(4-phenylphenyl)ethyl)amide;

- N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(4-benzoylphenyl)ethyl)amide;
- 5 *N*-(4-morpholinecarbonyl)-L-leucine(1*S*-cyano-2-(4-benzoylphenyl)ethyl)amide;
- N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(1-naphthyl)ethyl)amide;
- 10 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(1-naphthyl)ethyl)amide;
- 15 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(2-naphthyl)ethyl)amide;
- 20 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(2-naphthyl)ethyl)amide;
- 25 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(2-chlorophenyl)ethyl)amide;
- 30 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(2-chlorophenyl)ethyl)amide;
- 35 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(3,4-dichlorophenyl)ethyl)amide;
- 40 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyanobut-3-ynyl)amide;
- 45 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyanobut-3-ynyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine(1*S*-cyanopropyl)amide;
- N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(4-(2,6-dichloromethoxy)phenyl)ethyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(4-(2,6-dichloromethoxy)phenyl)ethyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2*S*-methylbutyl)amide;
- N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyanopentyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyanopentyl)amide;
- N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2,2-dimethylpropyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2,2-dimethylpropyl)amide;

- N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-3-methylbutyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-3-methylbutyl)amide;
- 5 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(4-nitrophenylethyl)amide;
- 10 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(4-nitrophenylethyl)amide;
- 15 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyanobutyl)amide;
- 20 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyanobutyl)amide;
- 25 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*R*-cyano-2*R*-benzyloxypropyl)amide;
- 30 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyanoethyl)amide;
- 35 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-3-(carbobenzyloxy)propyl)amide;
- 40 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-3-(carbobenzyloxy)propyl)amide;
- 45 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(3-benzimidazolyl)ethyl)amide;
- 50 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(3-benzimidazolyl)ethyl)amide;
- 55 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1-cyano-1-methylethyl)amide;
- 60 *N*-(4-morpholinecarbonyl)-L-leucine (1-cyano-1-methylethyl)amide;
- 65 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(4-hydroxyphenyl)ethyl)amide;
- 70 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(4-hydroxyphenyl)ethyl)amide;
- 75 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S,3*-dicyanopropyl)amide;
- 80 *N*-(4-morpholinecarbonyl)-L-leucine (1*S,3*-dicyanopropyl)amide;
- 85 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(4-hydroxy-3-iodophenyl)ethyl)amide;
- 90 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(4-hydroxy-3-iodophenyl)ethyl)amide;
- 95 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S,2*-dicyanoethyl)amide;
- 100 *N*-(4-morpholinecarbonyl)-L-leucine (1*S,2*-dicyanoethyl)amide;

- 5 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*R*-cyano-2-benzyloxyethyl)amide;
- 10 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(2-thienyl)ethyl)amide;
- 15 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(2-thienyl)ethyl)amide;
- 20 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-3-(methylsulfonyl)propyl)amide;
- 25 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-3-(methylsulfonyl)propyl)amide;
- 30 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-phenylethyl)amide;
- 35 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-phenylethyl)amide;
- 40 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-3-(4-hydroxyphenyl)propyl)amide;
- 45 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-3-(4-hydroxyphenyl)propyl)amide;
- 50 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-cyclohexylethyl)amide;
- 55 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-cyclohexylethyl)amide;
- 60 *N*-(4-morpholinecarbonyl)-L-phenylalanine (1*S*-cyano-2-(3-chlorophenyl)ethyl)amide;
- 65 and
- 70 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(3-chlorophenyl)ethyl)amide.

More preferred compounds of the invention include:

- 75 *N*-(4-morpholinecarbonyl)-L-(4-methyl)leucine (1*S*-cyano-3-phenylpropyl)amide;
- 80 *N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-benzyloxyethyl)amide;
- 85 *N*-(4-morpholinecarbonyl)-L-(4-methyl)leucine (1*R*-cyano-2-benzyloxyethyl)amide;
- 90 *N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2*R*-benzyloxypropyl)amide;
- 95 *N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(benzylsulfanyl)ethyl)amide;
- 100 *N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(2-chlorophenyl)methoxyethyl)amide;

- 5 *N*-(4-morpholinecarbonyl)-L-leucine (*1R*-cyano-2-(4-chlorophenyl)methyloxyethyl)amide;
- 10 *N*-(4-morpholinecarbonyl)-L-leucine (*1R*-cyano-2-(3-methoxyphenyl)methyloxyethyl)amide;
- 15 *N*-(4-morpholinecarbonyl)-L-(4-methyl)leucine (*1R*-cyano-2-(benzylsulfanyl)ethyl)amide;
- 20 *N*-(4-morpholinecarbonyl)-L-leucine (*1R*-cyano-2-(benzylsulfinyl)ethyl)amide;
- 25 *N*-(4-morpholinecarbonyl)-L-leucine (*1R*-cyano-2-((4-methoxyphenyl)methylsulfanyl)ethyl)amide;
- 30 *N*-(4-morpholinecarbonyl)-L-leucine (*1R*-cyano-2-(3-chlorophenyl)methyloxyethyl)amide;
- 35 *N*-(5-dimethylaminonaphth-1-ylsulfonyl)-L-leucine (*1R*-cyano-2-benzylmethyloxyethyl)amide;
- 40 *N*-(4-morpholinecarbonyl)-L-leucine (*1R*-cyano-2-(2-methylphenyl)methyloxyethyl)amide;
- 45 *N*-(4-morpholinecarbonyl)-L-leucine (*1R*-cyano-2-(3-methylphenyl)methyloxyethyl)amide;
- 50 *N*-(4-morpholinecarbonyl)-L-leucine (*1R*-cyano-2-(4-methylphenyl)methyloxyethyl)amide;
- 55 *N*-(4-morpholinecarbonyl)-L-leucine (*1R*-cyano-2-(3-carbomethoxyphenyl)methyloxyethyl)amide;
- 60 *N*-(4-morpholinecarbonyl)-L-leucine (*1R*-cyano-2-(4-carbomethoxyphenyl)methyloxyethyl)amide;
- 65 *N*-(4-morpholinecarbonyl)-L-leucine (*1S*-cyano-3-(carbo-*t*-butoxy)propyl)amide;
- 70 *N*-(4-morpholinecarbonyl)-L-leucine (*1S*-cyano-3-phenylpropyl)amide;
- 75 *N*-(4-Morpholinecarbonyl)-L-leucine-[*1S*(benzthiazol-2-ylcarbonyl)-3-phenylpropyl]amide;
- 80 *N*-(4-Morpholinecarbonyl)-L-leucine [*1S*-cyano-5-((benzyloxycarbonyl)-amino)-pentyl]amide;

- N-(4-Morpholinecarbonyl)-L-leucine-[1R,S(benzoxazol-2-ylcarbonyl)-3-phenylpropyl]amide;
- 5 *N*-(4-morpholinecarbonyl)-L-leucine [[1-[(6-phenylcarbamoyl)benzothiazol-2-ylcarbonyl]-3-phenylpropyl]]amide;
- N-(4-Morpholinecarbonyl]-L-leucine-[[6-(carbomethoxy)-benzoxazol-2-ylcarbonyl]-3-phenylpropyl]amide;
- 10 *N*-(4-morpholinecarbonyl)-L-cyclohexylalanine (1*S*-cyano-3-phenylpropyl)amide;
- N-(4-morpholinecarbonyl)-L-cyclohexylalanine (1*R*-cyano-2-benzyloxyethyl)amide;
- 15 *N*-(4-morpholinecarbonyl)-L-nor-leucine (1*S*-cyano-3-phenylpropyl)amide;
- 15 *N*-(4-Morpholinecarbonyl]-L-leucine 1*RS*-((5-phenyloxazol-2-yl)carbonyl)-3-phenylpropylamide;
- 20 *N*-(4-Morpholinecarbonyl]-L-leucine 1*S*-(oxazol-2-ylcarbonyl)-3-phenylpropylamide;
- 20 *N*-(4-morpholinecarbonyl)-L-(4-methyl)leucine [1-(Benzothiazol-2-ylcarbonyl)-3-phenylpropyl]amide;
- 25 *N*-(4-morpholinecarbonyl)-L-(2-naphthyl)alanine (1*S*-cyano-3-phenylpropyl)amide;
- 25 *N*-(4-morpholinecarbonyl)-L-(2-chlorophenyl)alanine (1*S*-cyano-3-phenylpropyl)amide;
- N-Benzoyl-L-leucine (1*R*-cyano-2-benzyloxyethyl)amide;
- 30 *N*-(4-morpholinecarbonyl)-L-(O-methyl)tyrosine (1*S*-cyano-3-phenylpropyl)amide;
- N-(4-morpholinecarbonyl)-L-leucine(1*S*-cyano-2-(carbobenzyloxy)ethyl)amide;
- 35 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-1-phenylmethyl)amide;
- 35 *N*-(4-morpholinecarbonyl)-L-leucine (1-cyanocyclopropyl)amide;
- N-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(2-chlorophenyl)ethyl)amide;
- 40 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(4-(2,6-dichloromethoxy)phenyl)ethyl)amide;
- N-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-3-(carbobenzyloxy)propyl)amide;
- 45 *N*-(4-morpholinecarbonyl)-L-leucine (1*S,3*-dicyanopropyl)amide;

N-(4-morpholinecarbonyl)-L-leucine (1*S*,2-dicyanoethyl)amide;

N-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-3-(methylsulfonyl)propyl)amide;

5 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-3-(4-hydroxyphenyl)propyl)amide;

and

10 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-cyclohexylethyl)amide.

15

Any compounds of this invention containing one or more asymmetric carbon atoms may occur as racemates and racemic mixtures, single enantiomers, diastereomeric mixtures and individual diastereomers. All such isomeric forms of these compounds are expressly included in the present invention. Each stereogenic carbon may be in the R or S

20 configuration, or a combination of configurations.

Some of the compounds of formulas (I), (Ia) and formulas (II), (IIa) can exist in more than one tautomeric form. The invention includes all such tautomers.

25 It shall be understood by one of ordinary skill in the art that all compounds of the invention are those which are chemically stable.

The invention includes pharmaceutically acceptable derivatives of compounds of formulas (I), (Ia) and formulas (II), (IIa). A "pharmaceutically acceptable derivative" 30 refers to any pharmaceutically acceptable salt or ester of a compound of this invention, or any other compound which, upon administration to a patient, is capable of providing (directly or indirectly) a compound of this invention, a pharmacologically active metabolite or pharmacologically active residue thereof. A pharmacologically active metabolite shall be understood to mean any compound of the invention capable of being 35 metabolized enzymatically or chemically. This includes, for example, hydroxylated or oxidized derivative compounds of the invention.

In addition, the compounds of this invention include prodrugs of compounds of the formulas (I),(Ia) and formulas (II), (IIa). Prodrugs include those compounds that, upon simple chemical transformation, are modified to produce the compounds of the invention. Simple chemical transformations include hydrolysis, oxidation and reduction. Specifically, when a prodrug of this invention is administered to a patient, the prodrug may be transformed into a compound of formulas (I),(Ia) or formulas (II), (IIa), thereby imparting the desired pharmacological effect.

10

- In order that the invention herein described may be more fully understood, the following detailed description is set forth. As used herein, the following abbreviations are used:
- BOC or t-BOC is tertiary butoxycarbonyl;
 - t-Bu is tertiary butyl;
 - 15 DMF is dimethylformamide;
 - EtOAc is ethyl acetate;
 - THF is tetrahydrofuran;
 - Ar is argon;
 - TFA is trifluoroacetic acid;
 - 20 EDC is 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride.
 - HOBT is 1-hydroxybenzotriazole

Also, as used herein, each of the following terms, used alone or in conjunction with other terms, are defined as follows (except where noted to the contrary):

25

- The term "alkyl" refers to a saturated aliphatic radical containing from one to ten carbon atoms or a mono- or polyunsaturated aliphatic hydrocarbon radical containing from two to twelve carbon atoms, containing at least one double or triple bond, respectively. "Alkyl" refers to both branched and unbranched alkyl groups. Preferred alkyl groups are straight chain alkyl groups containing from one to eight carbon atoms and branched alkyl groups containing from three to eight carbon atoms. More preferred alkyl groups are

straight chain alkyl groups containing from one to six carbon atoms and branched alkyl groups containing from three to six carbon atoms. It should be understood that any combination term using an "alk" or "alkyl" prefix refers to analogs according to the above definition of "alkyl". For example, terms such as "alkoxy", "alkythio" refer to alkyl groups linked to a second group via an oxygen or sulfur atom. "Alkanoyl refers to an alkyl group linked to a carbonyl group (C=O).

The term "cycloalkyl" refers to the cyclic analog of an alkyl group, as defined above.

- 10 Preferred cycloalkyl groups are saturated cycloalkyl groups containing from three to eight carbon atoms, and more preferably three to six carbon atoms.

15 The term "aryl" refers to phenyl and naphthyl. "Aroyl" refers to an aryl group linked to a carbonyl group (C=O).

The term "halo" refers to a halogen radical selected from fluoro, chloro, bromo or iodo. Preferred halo groups are fluoro, chloro and bromo.

- 20 The term "heteroaryl" refers to a stable 5-8 membered (but preferably, 5 or 6 membered) monocyclic or 8-11 membered bicyclic aromatic heterocycle radical. Each heterocycle consists of carbon atoms and from 1 to 4 heteroatoms selected from the group consisting of nitrogen, oxygen and sulfur. As used herein, "nitrogen" and "sulfur" include any oxidized form of nitrogen and sulfur and the quaternized form of any basic nitrogen. The 25 heterocycle may be attached by any atom of the cycle, which results in the creation of a stable structure. Preferred heteroaryl radicals include, for example, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolizinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, indazolyl, benzimidazolyl, 30 benzthiazolyl, benzoxazolyl, purinyl, quinolizinyl, quinolinyl, isoquinolinyl, cinnolinyl,

phthalazinyl, quinazolinyl, quinoxalinyl, naphthyridinyl, pteridinyl, carbazolyl, acridinyl, phenazinyl, phenothiazinyl or phenoxazinyl,

- The term "heterocycle" refers to a stable 5-8 membered (but preferably, 5 or 6
5 membered) monocyclic or 8-11 membered bicyclic heterocycle radical which may be either saturated or unsaturated, and is non-aromatic. Each heterocycle consists of carbon atoms and from 1 to 4 heteroatoms selected from the group consisting of nitrogen, oxygen and sulfur. As used herein, "nitrogen" and "sulfur" include any oxidized form of nitrogen and sulfur and the quaternized form of any basic nitrogen. The heterocycle may
10 be attached by any atom of the cycle, which results in the creation of a stable structure. Preferred heterocycle radicals include, for example, pyrrolinyl, pyrrolidinyl, pyrazolinyl, pyrazolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, pyranyl, thiopyranyl, piperazinyl and indoliny.

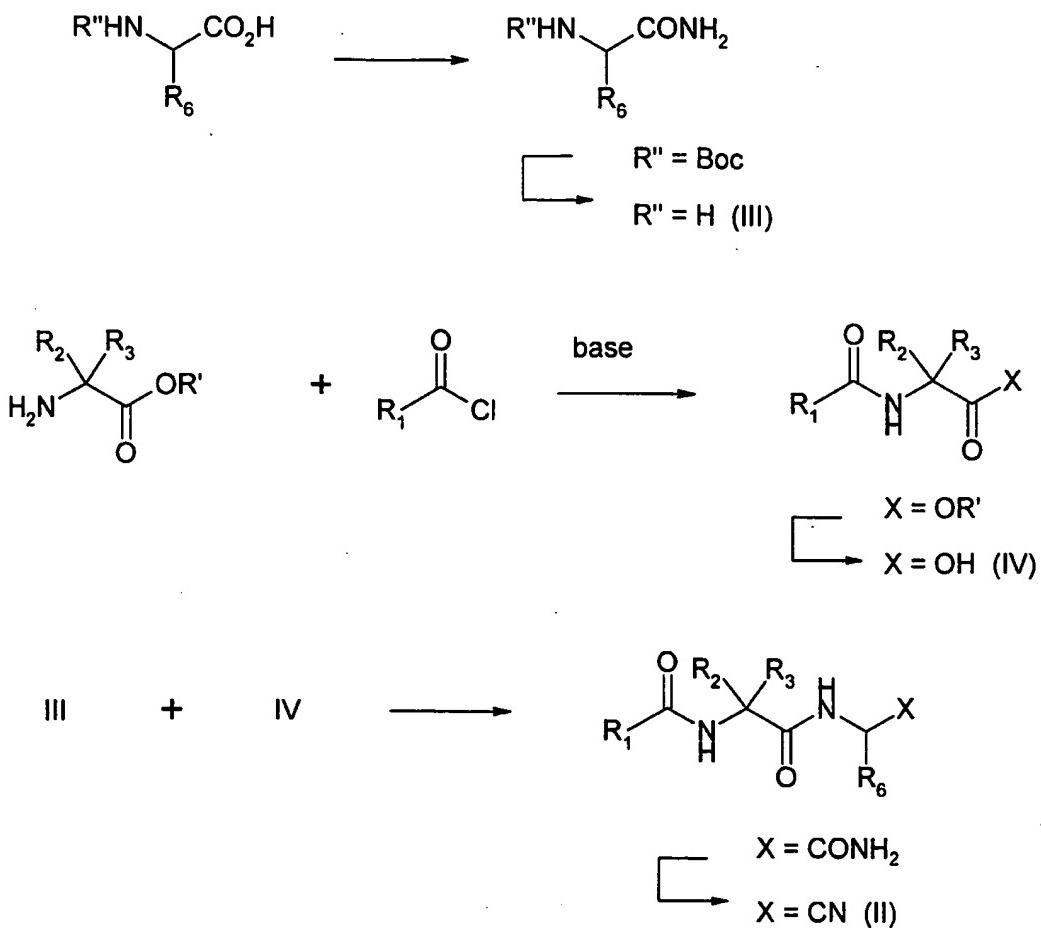
15

GENERAL SYNTHETIC METHODS

- The invention also provides processes of making the present novel compounds.
Compounds of the invention may be prepared by methods described below. Standard
20 peptide coupling, protection and deprotection reactions (see for example M. Bodanszky, The Practice of Peptide Synthesis, Springer-Verlag, 1984) are employed in these syntheses.

- Compounds of the invention having formula (II) or (IIa) (nitriles) may be prepared by
25 Method A (Scheme I)

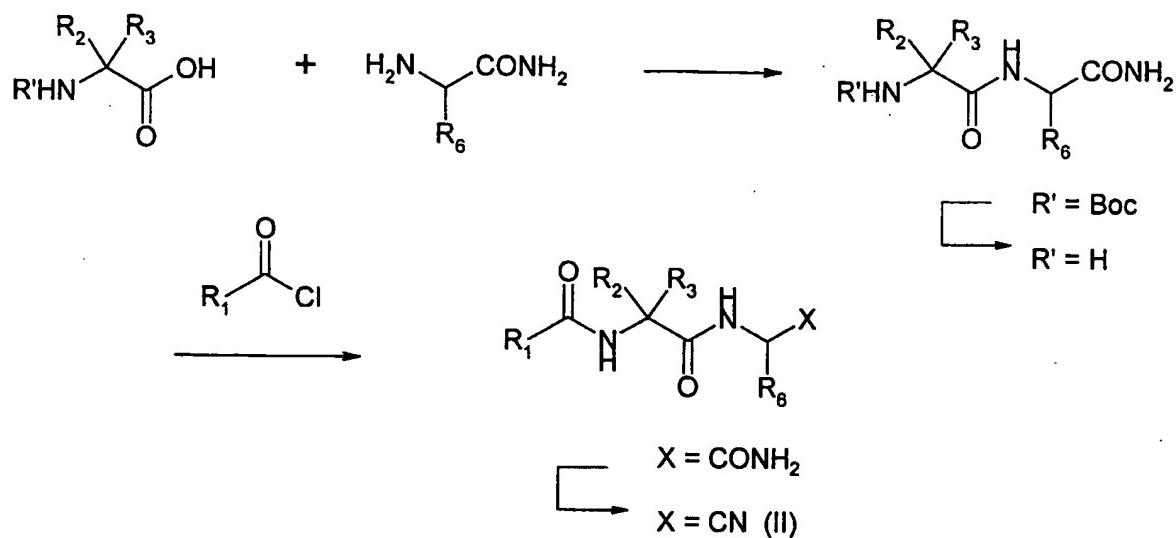
Scheme I (Method A)



According to Method A a suitably protected amino acid bearing R_6 is allowed to react with ammonia under standard coupling conditions. An example of a suitable protecting group is the *t*-butoxycarbonyl (Boc) group. An example of standard coupling conditions would be combining the starting materials in the presence of a coupling reagent such as 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide (EDC) with 1-hydroxybenzotriazole (HOBT), in a suitable solvent such as DMF or methylene chloride. A base such as N-methylmorpholine may be added. This is followed by deprotection to give amino acid amide III. An amino acid ester bearing R_2 and R_3 is then reacted with an acid chloride bearing R_1 in the presence of a suitable base such as N,N-diisopropylethylamine. Conversion to the carboxylic acid provides IV. Standard peptide coupling of III and IV, followed by dehydration of the amide provides the desired nitrile II or IIa. An example of suitable dehydration conditions is cyanuric chloride in DMF.

In a variation (Method B) illustrated in Scheme II, an amino acid amide bearing R₆ is coupled with an amine-protected amino acid bearing R₂ and R₃. A suitable protecting group and coupling conditions would be as described above. Deprotection is then followed by reaction with an acid chloride bearing R₁. Conversion of the amide to the nitrile as above provides II or IIa.

Scheme II (Method B)

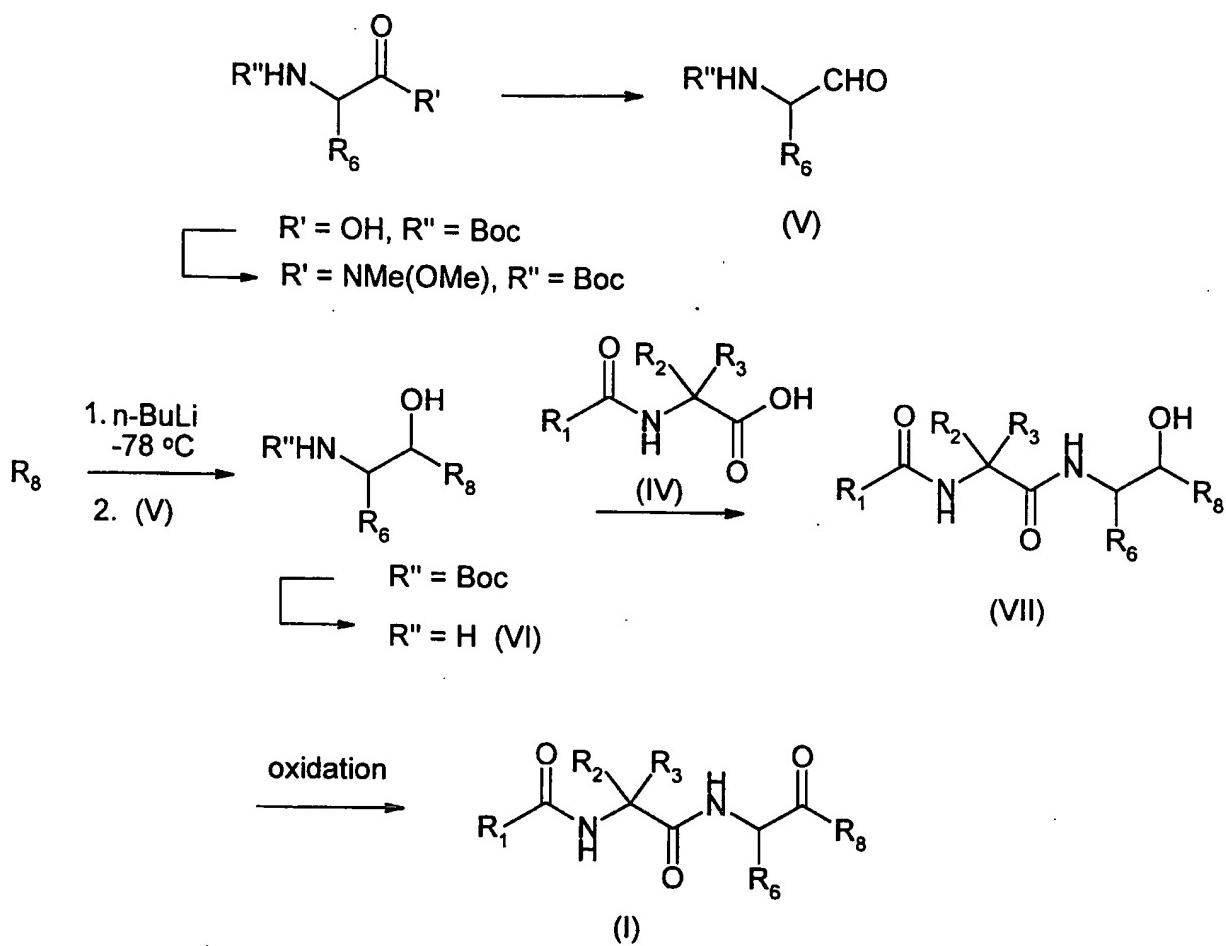


10

Compounds of the invention having formulas (I) or (Ia) (ketones) may be prepared by Methods C (Scheme III) or D (Scheme IV) as described below.

15

Scheme III (Method C)



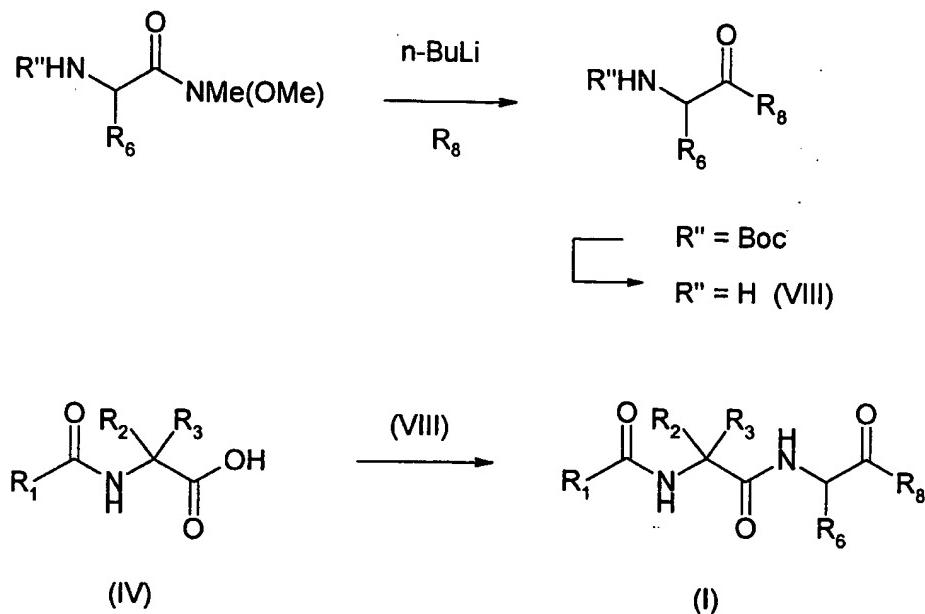
According to Method C, a suitably protected (for example Boc protected) amino acid is coupled with N,O-dimethylhydroxylamine under standard coupling conditions, such as with carbonyldiimidazole (CDI) in a solvent such as DMF, to give the corresponding amide. This is reduced to the aldehyde (V) with a suitable reducing agent such as LiAlH₄, in a suitable solvent such as THF.

- 10 The aldehyde (V) is reacted with the anion of a heterocycle **R**₈, which is generated by reacting **R**₈ with a strong base such as *n*-BuLi in a solvent such as THF at a temperature of about -30°C to -100°C and preferably at about -78°C . This is followed by removal of the protecting group providing alcohol (VI). This is coupled with (IV), prepared as described in Scheme I, under standard coupling conditions such as EDC and HOBT in

DMF in the presence of a base such as N-methylmorpholine to provide (VII). Oxidation of (VII) with, for example, the Dess Martin Reagent (1,1,1,-triacetoxy-1,1-dihydro-1,2-benziодoxol-3(1H)-one) in methylene chloride and t-BuOH, provides the desired ketone of formulas (I) or (Ia).

5

Scheme IV (Method D)



- 10 In Method D, a suitably protected amino acid N-methoxy-N-methylamide (prepared as described in Scheme III) is treated with the anion of a heterocycle R_8 , generated by reacting R_8 with a strong base such as $n\text{-BuLi}$ in a suitable solvent such as THF at a temperature of about -30 °C to -100 °C and preferably at about -78 °C. Deprotection of the resulting ketone provides (VIII). This is coupled with (IV), which is prepared as
- 15 described in Scheme I, under standard coupling conditions such as EDC and HOBT in DMF in the presence of a base such as N-methylmorpholine to provide the desired ketone of formulas (I) or (Ia).

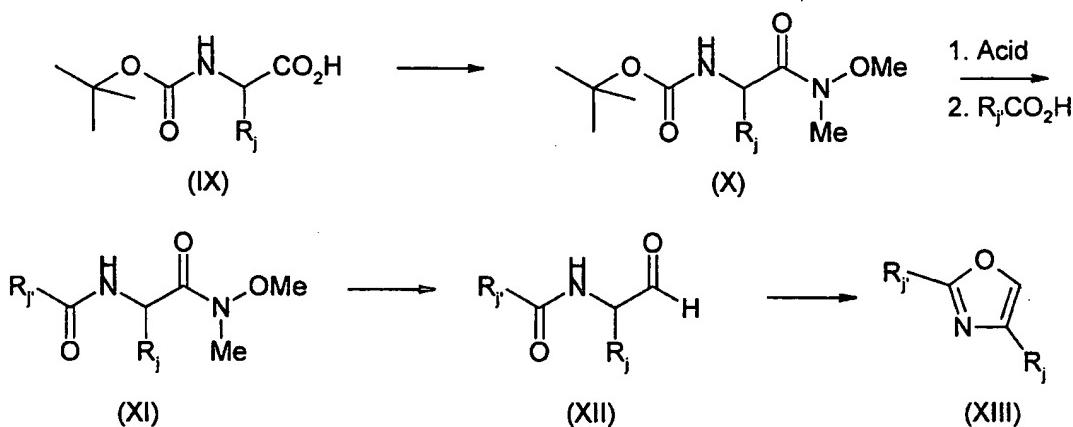
- Compounds of the invention where A is a bond (formulas I, Ia and II, IIa) could be
 20 prepared in analogous fashion to the Schemes above by using R_1X , where X = Br, Cl, or

I, instead of an acyl halide ($R_1C(O)Cl$) in Schemes I and II, or by using $R_1NHC(R_2)(R_3)CO_2H$ instead of (IV) in Schemes III and IV.

- Intermediates used in Schemes I-IV are either commercially available or easily prepared
 5 by methods known to those skilled in the art. A procedure (Method E) that is useful for preparing substituted oxazoles which may be used as R_8 in Scheme III and IV (Methods C and D) is illustrated below in Scheme V.

Scheme V (Method E)

10



- An N-protected amino acid, for example a *t*-Boc protected amino acid (IX) is coupled
 with N,O-dimethylhydroxylamine using a suitable coupling agent, such as
 15 carbonyldiimidazole (CDI), in a suitable solvent, such as CH_2Cl_2 , THF or DMF, at about
 0 °C to provide (X). The N-protecting group is then removed, for example the *t*-Boc
 group may be removed by treatment with a suitable acid, such as trifluoroacetic acid, in a
 suitable solvent, such as CH_2Cl_2 . The resulting amine is coupled with the desired
 carboxylic acid using suitable coupling conditions, such as EDC with HOBT in a suitable
 20 solvent such as DMF, in the presence of a base such as N-methylmorpholine to provide a
 diamide (XI). The N-methoxy-methyl amide is then treated with a suitable reducing
 agent, such as $LiAlH_4$ in a suitable solvent, such as THF, to provide an aldehyde (XII).
 Cyclodehydration (see for example P.Wipf and S. Lim, J. Amer. Chem. Soc., 1995, 117,
 558) of (XII) with triphenylphosphine and hexachloroethane in a suitable solvent, such

as acetonitrile in the presence of a suitable base, such as Et₃N provides the desired oxazole (XIII).

Desired disubstituted thiazoles, which may be used as R₈ in Scheme III and IV (Method 5 C and D) may be prepared by the Hantzsch method in which a thioamide is condensed with an alpha-halocarbonyl compound. This method is known to those skilled in the art and is well-documented in the chemical literature (for example, J. Metzger and E.J. Vincent, The Chemistry of Heterocyclic Compounds, Vol. 34, 1979; A.R. Katritzky et al., J. Org. Chem., 1995, 60, 5638; R. Flaig and H. Hartmann, Heterocycles, 1997, 45, 10 875).

METHODS OF THERAPEUTIC USE

15 The compounds of this invention effectively block degradation of the invariant chain to CLIP by cathepsin S, and thus inhibit antigen presentation and antigen-specific immune responses. Control of antigen specific immune responses is an attractive means for treating autoimmune diseases and other undesirable T-cell mediated immune responses. Thus, there is provided methods of treatment using the compounds of this invention for 20 such conditions. These encompass autoimmune diseases including, but not limited to, rheumatoid arthritis, systemic lupus erythematosus, Crohn's disease, ulcerative colitis, multiple sclerosis, Guillain-Barre syndrome, psoriasis, Grave's disease, myasthenia gravis, scleroderma, glomerulonephritis, atopic dermatitis and insulin-dependent diabetes mellitus. The compounds of the invention can also be used to treat other disorders 25 associated with extracellular proteolysis such as Alzheimer's disease. The compounds of the invention can also be used to treat other disorders associated with inappropriate autoimmune responses, T-cell mediated immune responses, or extracellular proteolysis mediated by cathepsin S, unrelated to those listed above or discussed in the Background of the Invention. Therefore, the invention also provides methods of modulating an 30 autoimmune disease comprising administering to a patient in need of such treatment a pharmaceutically effect amount of a compound according to the invention.

For therapeutic use, the compounds of the invention may be administered in any conventional dosage form in any conventional manner. Routes of administration include, but are not limited to, intravenously, intramuscularly, subcutaneously, intrasynovially, by infusion, sublingually, transdermally, orally, topically or by inhalation. The preferred modes of administration are oral and intravenous.

The compounds of this invention may be administered alone or in combination with adjuvants that enhance stability of the inhibitors, facilitate administration of pharmaceutical compositions containing them in certain embodiments, provide increased dissolution or dispersion, increase inhibitory activity, provide adjunct therapy, and the like, including other active ingredients. Advantageously, such combination therapies utilize lower dosages of the conventional therapeutics, thus avoiding possible toxicity and adverse side effects incurred when those agents are used as monotherapies. Compounds of the invention may be physically combined with the conventional therapeutics or other adjuvants into a single pharmaceutical composition. Advantageously, the compounds may then be administered together in a single dosage form. In some embodiments, the pharmaceutical compositions comprising such combinations of compounds contain at least about 15%, but more preferably at least about 20%, of a compound of formulas (I), (Ia), (II) or (IIa) (w/w) or a combination thereof. Alternatively, the compounds may be administered separately (either serially or in parallel). Separate dosing allows for greater flexibility in the dosing regime.

As mentioned above, dosage forms of the compounds of this invention include pharmaceutically acceptable carriers and adjuvants known to those of ordinary skill in the art. These carriers and adjuvants include, for example, ion exchangers, alumina, aluminum stearate, lecithin, serum proteins, buffer substances, water, salts or electrolytes and cellulose-based substances. Preferred dosage forms include, tablet, capsule, caplet, liquid, solution, suspension, emulsion, lozenges, syrup, reconstitutable powder, granule, suppository and transdermal patch. Methods for preparing such dosage forms are known (see, for example, H.C. Ansel and N.G. Popovish, *Pharmaceutical Dosage Forms and*

Drug Delivery Systems, 5th ed., Lea and Febiger (1990)). Dosage levels and requirements are well-recognized in the art and may be selected by those of ordinary skill in the art from available methods and techniques suitable for a particular patient. In some embodiments, dosage levels range from about 10-1000 mg/dose for a 70 kg patient.

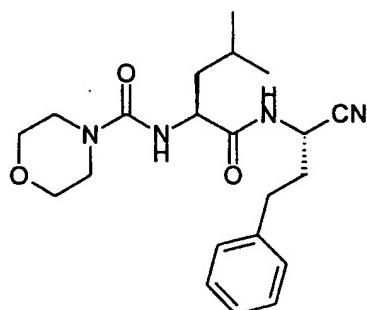
- 5 Although one dose per day may be sufficient, up to 5 doses per day may be given. For oral doses, up to 2000 mg/day may be required. As the skilled artisan will appreciate, lower or higher doses may be required depending on particular factors. For instance, specific dosage and treatment regimens will depend on factors such as the patient's general health profile, the severity and course of the patient's disorder or disposition
10 thereto, and the judgment of the treating physician.

15

SYNTHETIC EXAMPLES

EXAMPLE 1

- 20 **Morpholine-4-carboxylic acid [1-(*S*)-(1-*(S*)-cyano-3-phenylpropylcarbamoyl)-3-methylbutyl] amide**



- As outlined generally in Scheme I (Method A), *N*-Boc-L-homophenylalanine (0.50 g, 1.79 mmol) was dissolved in 20 mL of DMF which was cooled with an ice-water bath.
25 1-Hydroxybenzotriazole (HOBT) (0.29 g, 2.14 mmol) and EDC (0.41 g, 2.00 mmol)

were added followed by stirring for 20 min. Ammonium hydroxide was added (0.5 mL) and stirring was continued overnight (16 h). The reaction mixture was diluted with 50 mL of methylene chloride to give a white precipitate. The mixture was filtered and the filtrate was washed with brine (100 mL) followed by saturated bicarbonate (100 mL).

- 5 The organic layer was dried over MgSO₄, filtered and concentrated by rotary evaporation to give the corresponding amide (0.45 g, 90%) that was used without further purification.

Benzyl L-leucine p-toluenesulfonate salt (8.00 g, 20.3 mmol) was dissolved in 20 mL of DMF followed by addition of N,N-diisopropylethylamine (10.61 mL, 60.9 mmol) and

- 10 stirring under Ar for 15 min. 4-Morpholinecarbonyl chloride (4.55 g, 30.4 mmol) was added and stirring was continued overnight (16 h). The solution was diluted with 500 mL of EtOAc and washed with 3 x 500 mL of water. The organic layer was dried over MgSO₄, filtered and concentrated by rotary evaporation to 8.01 g of the crude product. The product was purified by flash chromatography (SiO₂, 40% EtOAc/hexane) resulting
15 in a thick oil. This oil (18 g, 53.8 mmol) was dissolved in ethanol (500 mL). Pd(OH)₂ (642 mg) was added followed by cyclohexene (100 mL). The mixture was refluxed for 45 min at which time TLC indicated consumption of the benzyl ester. The reaction was cooled and filtered through diatomaceous earth and evaporated to dryness to give N-(4-morpholinecarbonyl)-L-leucine as a very thick oil (13 g, 99%) that was used without
20 further purification.

N-Boc-L-homophenylalaninamide (from the first paragraph) (114 mg, 0.41 mmol) was dissolved in 10 mL of CH₂Cl₂ and 10 mL of trifluoroacetic acid (TFA) was added.

- Stirring was continued for 30 min at which time the reaction mixture was evaporated to
25 dryness giving the TFA salt of L-homophenylalanine amide. N-(4-morpholinecarbonyl)-L-leucine (100 mg, 0.41 mmol), from above, was dissolved in 10 mL of DMF and cooled by an ice-water bath. HOBT (72 mg, 0.53 mmol) and EDC (102 mg, 0.53 mmol) were added and the mixture was stirred at 0 °C for 15 min. To the cold solution was added the TFA salt of L-homophenylalaninamide as a solution in 5 mL of DMF, followed by
30 addition of N-methylmorpholine (94 µL, 0.86 mmol). The ice bath was removed and the reaction was stirred at ambient temperature overnight (16 h). The reaction was diluted

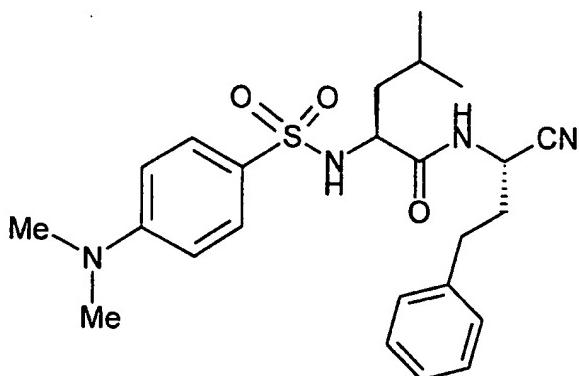
with 50 mL of CH₂Cl₂ to give a white precipitate. The mixture was filtered and the solid washed with an additional 50 mL of CH₂Cl₂. The filtrates were combined and washed with saturated bicarbonate (100 mL), 1 N HCl (100 mL) and brine (2 x 100 mL). The organic layer was dried over MgSO₄ and concentrated by rotary evaporation to give an
5 oily residue. The residue was chromatographed (SiO₂, 5% MeOH in CH₂Cl₂) to give the a white solid (130 mg, 78%).

This amide (150 mg, 0.37 mmol) (material from more than one reaction) was dissolved in 2 mL of DMF and cooled to 0 °C with an ice-water bath. To the solution was added
10 cyanuric chloride (46 mg, 0.37 mmol). The ice bath was removed and the reaction stirred to ambient temperature over the next hour. During the course of the reaction a white precipitate formed. The reaction was diluted with 100 mL of EtOAc and washed with 100 mL of water (3x). The organic layer was dried over MgSO₄, filtered and concentrated by rotary evaporation to give the crude residue. The residue was purified by
15 chromatography (SiO₂, 40% hexane in EtOAc) to give the title compound as a hard white glass (120 mg, 84%). ¹H NMR (270 MHz, CDCl₃): δ 8.00-7.87 (1H, m), 7.35-7.13 (3H, m), 7.12-7.05 (2H, m), 5.10-5.02 (1H, m), 4.80-4.60 (1H, m), 4.45-4.20 (1H, m), 3.75-3.50 (4H, m), 3.45-3.30 (4H, m), 2.80-2.60 (2H, m), 2.10-1.90 (2H, m), 1.70-1.45 (3H, m), 1.05-0.90 (6H, m).

20

EXAMPLE 2

25 **2-(S)-(4-Dimethylaminobenzenesulfonylamino)-4-methylpentanoic acid (1-(S)-cyano-3-phenylpropyl) amide**



NH_4OH (4 mL) was added to a premixed (15 min) solution of *N*-(*t*-butoxycarbonyl)-L-homophenylalanine (4.00 g, 14.3 mmol), EDC (3.24 g, 17.2 mmol), and HOBT (2.32 g, 17.2 mmol) in DMF (20 mL) at room temperature. After 16 h the reaction mixture was

- 5 diluted with CH_2Cl_2 and filtered, washed sequentially with 10% aqueous HCl, satd. NaHCO_3 , H_2O ($\times 3$), brine, dried over Na_2SO_4 , and concentrated giving *N*-(*t*-butoxycarbonyl)-L-homophenylalaninamide (3.10 g, 78%) as a white solid.

TFA (2.5 mL) was added to a solution of *N*-(*t*-butoxycarbonyl)-L-

- 10 homophenylalaninamide (1.00 g, 3.59 mmol) in CH_2Cl_2 (10 mL) at room temperature. After stirring for 0.5 h the reaction mixture was concentrated giving a colorless oil. As described generally by Scheme II, Method B, the oil was dissolved in CH_2Cl_2 (10 mL) and *N,N*-diisopropylethylamine (1.90 g, 14.4 mmol) and added to a premixed (15 min) solution of *N*-(*t*-butoxycarbonyl)-L-leucine (913 mg, 3.95 mmol), EDC (826 mg, 4.30 mmol), HOBT (581 mg, 4.30 mmol) in CH_2Cl_2 (10 mL) at room temperature. After stirring for 16 h the reaction was quenched by the addition of H_2O , diluted with EtOAc, washed sequentially with 10% aqueous HCl, satd. NaHCO_3 , H_2O brine, dried over Na_2SO_4 , and concentrated giving 1.3 g of a white solid. The crude solid was triturated with 5%EtOAc/Hexane giving *N*-[*N*-(*t*-butoxycarbonyl)-L-leucinyl]-L-
- 15 homophenylalaninamide (1.1 g, 78%) as a white solid.
- 20

TFA (2.5mL) was added to a solution of *N*-[*N*-(*t*-butoxycarbonyl)-L-leucinyl]-L-homophenylalaninamide (500 mg, 1.28 mmol) in CH_2Cl_2 (10 mL) at room temperature. After stirring for 0.5 h the reaction mixture was concentrated giving a colorless oil which

was diluted with CH₂Cl₂ (2.5 mL). Diisopropylethylamine (588 mg, 4.55 mmol) and *p*-Me₂NC₆H₄SO₂Cl [prepared by the reaction of *p*-Me₂NC₆H₄SO₃Na⁺ (1.0 g, 4.48 mmol) with thionyl chloride and pyridine (1 mL) at 55 °C for 2 h followed by cooling, diluting with toluene and concentrating to give *p*-Me₂NC₆H₄SO₂Cl.] was added at room
5 temperature. After stirring for 16 h the reaction was quenched by the addition of H₂O, diluted with EtOAc, washed sequentially with 10% aqueous HCl, satd. NaHCO₃, H₂O (x3), brine, dried over Na₂SO₄, and concentrated giving a yellow solid (408 mg). The crude residue was fractionated by flash chromatography (25-100% EtOAc/Hexane) giving *N*-[*N*-(4-dimethylaminophenyl)sulfonyl]-L-leucinyl]-L-homophenylalaninamide
10 (90 mg, 15%) as a white solid. Some title compound (60 mg, 10%) was isolated from this reaction as well.

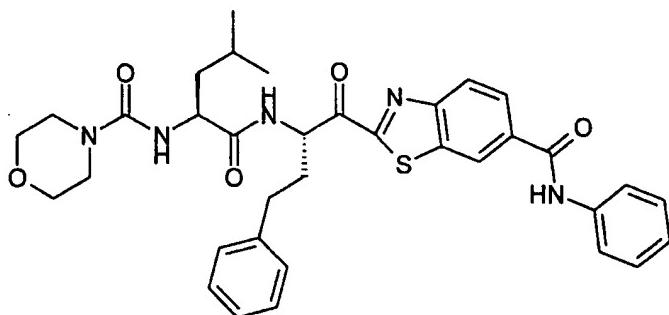
Cyanuric chloride (33 mg, 0.18 mmol) was added to a solution of *N*-[*N*-(4-dimethylaminophenyl)sulfonyl]-L-leucinyl]-L-homophenylalaninamide (80 mg, 0.18
15 mmol) in DMF (2 mL) at 0 °C. After stirring for 2h, the reaction was quenched by addition of satd. NaHCO₃, filtered, diluted with EtOAc, washed sequentially with H₂O (x5), brine, dried over Na₂SO₄, and concentrated giving a yellow foam. The crude residue was fractionated by preparative HPLC (65% AcCN/H₂O/0.1%TFA) giving the title compound (47 mg, 57%) as a white solid, m.p. 46-48 °C. ¹H NMR (400 MHz, CDCl₃): δ:
20 7.74(2H, d, *J*= 9), 7.37-7.34 (2H, m), 7.30-7.26 (2H, m), 7.23-7.21 (3H, m), 6.79 (1H, d, *J*=8.5), 4.91 (1H, bs), 4.70 (1H, ddd, *J*=8, 8, 8), 3.68-3.73 (1H,m), 3.06 (3H, s), 2.84-2.76 (2H, m), 2.16-2.09(2H, m), 1.63-1.56 (2H,m), 1.42-1.37 (1H, m), 0.88 (3H, d, *J*=6), 0.71 (3H, d, *J*=6).

25

EXAMPLE 3

2-(2-(*S*)-{4-Methyl-2-(*S*)-[(morpholine-4-carbonyl)amino]pentanoylamino}-4-phenylbutyryl)benzothiazole-6-carboxylic acid phenylamide

30



- As described generally in Method C, N-(t-Boc)-L-homophenylalanine (10.0 g, 35.8 mmol) was dissolved in 50 mL of DMF. The solution was cooled to 0 °C with an ice-water bath. Carbonyldiimidazole (6.4 g, 39.4 mmol) was added to the reaction solution followed by N-methylmorpholine (3.9 g, 39.4 mmol). The reaction was stirred for 1 h at which time N,O-dimethylhydroxylamine hydrochloride (3.8 g, 39.4 mmol) was added. The ice bath was removed and the reaction was stirred at ambient temperature for 3 h. The reaction solution was poured into 200 mL of 1N HCl and extracted with 200 mL of EtOAc. The organic layer was washed with 2 x 100 mL of 1N HCl, 100 mL of saturated sodium bicarbonate, 2 x 100 mL water, and 2 x 100 mL brine. The organic layer was dried over Na₂SO₄, decanted and concentrated by rotary evaporation to give the desired amide as a thick oil (11.1 g, 96% crude) which was used without further purification.
- The amide (3.7 g, 11.5 mmol), dissolved in 20 mL THF was added dropwise over 20 min to a suspension of LiAlH₄ (0.53 g, 13.9 mmol) in 60 mL THF which was cooled to 0 °C in an ice-water bath. The mixture was stirred for 15 min, then quenched with 10 mL of a saturated solution of sodium bicarbonate, diluted with 200 mL water and extracted with 3x100 mL EtOAc. The organic layers were combined and washed with 100 mL 1 N HCl and 2 x 100 mL brine. The organic layer was dried over Na₂SO₄, filtered over a pad of diatomaceous earth and concentrated by rotary evaporation. The residue was purified by flash chromatography (SiO₂, 5% i-PrOH in CH₂Cl₂) to give the desired aldehyde as an oily solid (2.4 g, 79%).

To a dry 100 mL flask was added 6-(phenylcarbamoyl)benzothiazole (0.58 g, 2.3 mmol) and THF (12 mL). The reaction mixture was cooled to -78 °C with a dry-ice/acetone bath. n-BuLi (2.5 M in hexanes) (1.8 mL, 4.5 mmol) was added dropwise to the reaction mixture. The reaction was stirred for 20 min to give a suspension. A solution of the above aldehyde (200 mg, 0.75 mmol) in 3 mL of dry THF was added all at once via syringe. The temperature was gradually increased to -40 °C and the reaction was stirred for 3 h at which time TLC showed consumption of the aldehyde. The reaction was quenched at -78 °C by the addition of a saturated solution of NH₄Cl and the product was extracted with 50 mL EtOAc. The organic layer was dried over MgSO₄, filtered and concentrated to give a residue that was purified by chromatography (SiO₂, 2% MeOH in CH₂Cl₂) to give the desired alcohol as a solid (194 mg, 50%).

N-(4-morpholinecarbonyl)-L-leucine (26.4 mg, 0.11 mmol) (prepared as described in Example 1) was dissolved in 2 mL of DMF. The solution was cooled to 0 °C with an ice-water bath and HOBT (19 mg, 0.14 mmol) and EDC (27 mg, 0.14 mmol) were added and the solution stirred for 20 min. The TFA salt of the N-deprotected alcohol from above (prepared by stirring the above N-Boc protected alcohol in methylene chloride with TFA at room temperature for 30 min and evaporation to dryness) (57 mg, 0.11 mmol of *N*-Boc precursor) was added to the reaction as a solution in 1 mL of DMF followed by addition of *N*-methylmorpholine (35 µL, 0.32 mmol). The reaction was stirred for 3 h, diluted with EtOAc and washed with 10 mL 1N HCl and 10 mL saturated bicarbonate and 2 x 100 mL brine. The organic layer was dried over MgSO₄, filtered and concentrated. The residue was purified by chromatography (SiO₂, 2% MeOH in CH₂Cl₂) to give the desired coupled product as a white solid (57 mg, 82%).

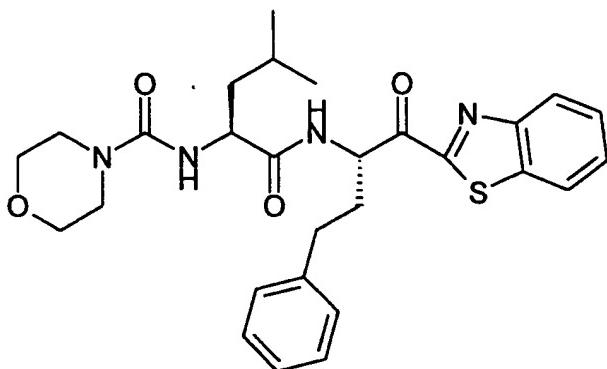
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To the above product (50.4 mg, 0.08 mmol) was added the Dess-Martin periodinane (133 mg, 0.31 mmol), 10 mL CH₂Cl₂ and 4 mL t-BuOH. The reaction mixture was allowed to stir overnight at room temperature. It was then was diluted with 20 mL CH₂Cl₂, washed with 20 mL of saturated solution of Na₂S₂O₃ and 20 mL NaHCO₃ solution, the organic layer was washed with brine, dried over MgSO₄, filtered and concentrated. The residue was purified by chromatography (SiO₂, 2% MeOH in CH₂Cl₂) to give the title compound

as a white solid (30 mg, 60%). ^1H NMR (270 MHz, CDCl_3): δ 8.77-8.70 (1H, m), 8.57-8.52 (1H, m), 8.28-8.20 (1H, m), 8.15-8.07 (1H, m), 7.78-7.68 (2H, m), 7.45-7.35 (2H, m), 7.29-7.05 (7H, m), 5.75-5.65 (1H, m), 5.00-4.92 (1H, m), 4.54-4.41 (1H, m), 3.74-3.58 (4H, m), 3.40-3.24 (4H, m), 2.78-2.62 (2H, m), 2.51-2.32 (1H, m), 2.21-2.02 (1H, m), 1.90-1.40 (3H, m), 1.00-0.80 (6H, m).

EXAMPLE 4

10 **Morpholine-4-carboxylic acid {1-(S)-[1-(S)-(benzothiazole-2-carbonyl)-3-phenylpropylcarbamoyl]-3-methylbutyl} amide**



15 Dry THF (1.5 mL), under Ar, was cooled to -78°C with a dry-ice/acetone bath. n-BuLi (2.0 M in hexanes) (698 μL , 1.40 mmol) was added to reaction flask followed by dropwise addition of freshly distilled benzothiazole (180 mg, 1.40 mmol) as a solution in 0.5 mL of dry THF. The reaction was stirred for 15 min to give a suspension. A solution of *N*-(*t*-butoxycarbonyl)-(*N'*-methyl-*N'*-methoxy)-L-homophenylalaninamide (300 mg, 0.930 mmol) (prepared as described in Example 3) in 1 mL of dry THF was added all at once via syringe. The reaction was stirred for 5 min at which time TLC showed consumption of the amide. The reaction was quenched by the addition of water and the product extracted with 50 mL of EtOAc. The organic layer was dried over MgSO_4 ,

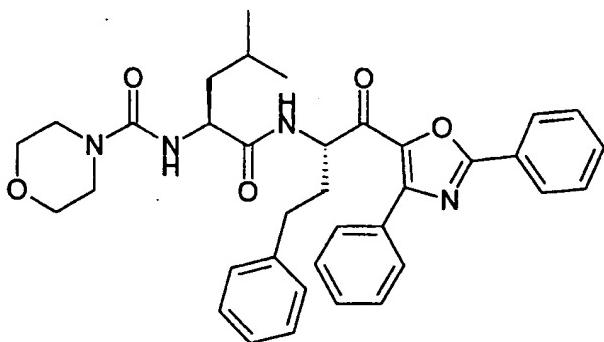
filtered and concentrated to give a residue that was purified by preparative TLC (CH_2Cl_2) to give the desired ketone as a clear colorless oil.

N-(4-morpholinecarbonyl)-L-leucine (82 mg, 0.34 mmol) (prepared as described in
5 Example 1) was dissolved in 2 mL of DMF. The solution was cooled to 0 °C with an ice-water bath and HOBT (60 mg, 0.44 mmol) and EDC (83 mg, 0.44 mmol) were added and the solution stirred for 20 min. The TFA salt of the N-deprotected ketone from above (prepared by stirring the above N-Boc protected alcohol in methylene chloride with TFA at room temperature for 30 min and evaporation to dryness) (133 mg, 0.34 mmol of *N*-
10 Boc precursor) was added to the reaction as a solution in 1 mL of DMF followed by addition of *N*-methylmorpholine (77 μ L, 0.70 mmol). The reaction was stirred for 3 h, diluted with EtOAc and washed with 100 mL 1N HCl and 100 mL saturated bicarbonate and 2 x 100 mL brine. The organic layer was dried over MgSO_4 , filtered and concentrated. The residue was purified by chromatography (SiO_2 , 50% EtOAc in
15 hexane) to give the title compound as a white solid (40 mg, 23%) that was shown to be a 1 to 1 mixture of two epimers. ^1H NMR (270 MHz, CDCl_3): δ 8.15-8.08 (1H, m), 7.98-7.88 (1H, m), 7.60-7.40 (2H, m), 7.25-7.07 (5H, m), 7.02-6.92 (1H, m), 5.90-5.75 (1H, m), 4.98-4.90 (1H, m), 4.50-4.35 (1H, m), 3.66-3.57 (4H, m), 3.40-3.30 (4H, m), 2.80-2.70 (2H, m), 2.50-2.35 (1H, m), 2.25-2.10 (1H, m), 1.80-1.40 (3H, m), 1.00-0.88 (6H,
20 m).

EXAMPLE 5

25

Morpholine-4-carboxylic acid {1-(*S*)-[1-(*S*)-(2,4-diphenyloxazole-5-carbonyl)-3-phenylpropylcarbamoyl]-3-methylbutyl} amide



- As outlined generally in Scheme IV (Method D), 2,4-diphenyloxazole (361 mg, 1.63 mmol) in 15 mL dry THF was cooled to -78 °C and *n*-butyllithium (1.16 mL of a 1.4 M solution, 1.63 mmol) was added. After stirring for 1 h at -78 °C, a solution of the free base of *N*-[*N*-(*t*-butoxycarbonyl)-L-leucinyl]-L-homophenylalaninamide (prepared as described in Example 3) in 5 mL of dry THF was added dropwise. The temperature of the reaction mixture was allowed to rise to -20 °C and maintained for 2 h after which time the reaction mixture was quenched with 100 mL of NH₄Cl (10% aqueous) and extracted with 3 x 100 mL EtOAc. The combined extracts were washed with 2 x 100 mL brine, dried with Na₂SO₄, filtered and concentrated. The resulting residue was purified by chromatography (florisil, 15% - 20% hexane in EtOAc) yielding 190 mg (72%) of [1-(2,4-diphenyloxazole-5-carbonyl)-3-phenylpropyl]carbamic acid tert-butyl ester.
- N*-[(4-Morpholinyl)carbonyl]-L-leucine (100 mg, 0.35 mmol) (prepared as described in Example 1) was dissolved in 10 mL DMF and cooled to 0 °C. To the solution was added EDC (77 mg, 0.4 mmol) and HOBr (54 mg, 0.4 mmol) and the reaction was stirred for 1h. In a separate flask, [1-(2,4-diphenyloxazole-5-carbonyl)-3-phenylpropyl]carbamic acid tert-butyl ester (158 mg, 0.31 mmol) was dissolved in 4 mL CH₂Cl₂ and 2 mL TFA was added. After stirring for 1 h, the solvents were evaporated, the residue was dissolved in 5 mL DMF and N-methylmorpholine (406 mg, 0.4 mmol) was added. The resulting solution was added to the previously prepared solution of activated leucine derivative at 0 °C. The reaction mixture was stirred at room temperature for 3 h, cooled to 0 °C, and quenched with 100 mL of a 10% solution of citric acid in water. The resulting mixture was extracted with 3 x 100 mL EtOAc. The combined organic extracts were washed with

2 x 100 mL of saturated bicarbonate and 1 x 100 mL brine. The organic layer was dried over Na₂SO₄, filtered and concentrated to a residue that was purified by chromatography (florisil, 30% - 50% EtOAc in hexane) to give the title compound as a white solid (90mg, 84%), m.p. 83-5 °C, MS (ES) 609 (M⁺).

5

The following compounds were also prepared using the procedure described in Example 5:

10 Morpholine-4-carboxylic acid {1-(S)-[1-(S)-(2,4-diphenyl-oxazole-5-carbonyl)-3-phenyl-propylcarbamoyl]-3,3-dimethylbutyl} amide, m.p. 95-7 °C, MS (ES) 623 (M⁺).

15 Morpholine-4-carboxylic acid {2-cyclohexyl-1-(S)-[1-(S)-(2,4-diphenyl-oxazole-5-carbonyl)-3-phenyl-propylcarbamoyl]-ethyl} amide, m.p. 93-5 °C, MS (ES) 649 (M⁺).

Morpholine-4-carboxylic acid {1-(S)-[2,4-diphenyl-oxazole-5-yl)-2-oxo-ethylcarbamoyl]-3-methylbutyl} amide, m.p. 155-7 °C, MS (ES) 505 (M⁺).

20 Morpholine-4-carboxylic acid {2-cyclohexyl-1-(S)-[2-(2,4-diphenyl-oxazol-5-yl)-2-oxo-ethylcarbamoyl]-ethyl}-amide, m.p. 122-3 °C, MS (ES) 545 (M⁺).

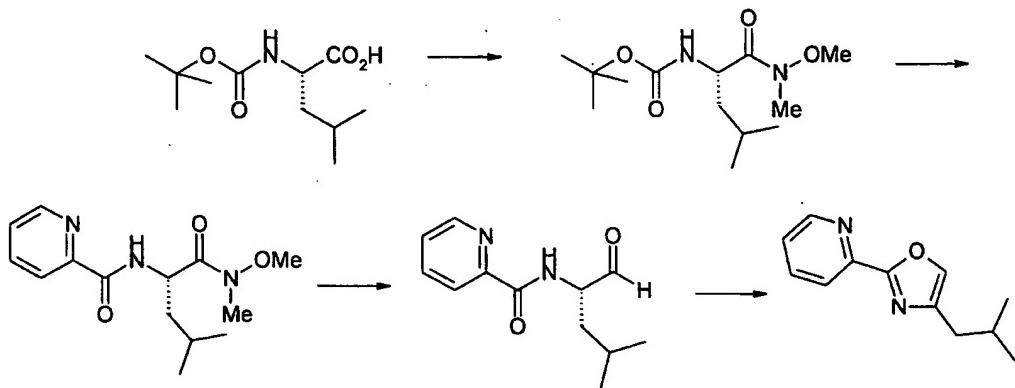
Morpholine-4-carboxylic acid {1-(S)-[2-(2,4-diphenyl-oxazol-5-yl)-2-oxo-ethylcarbamoyl]-3,3-dimethylbutyl}-amide, m.p. 97-9 °C, MS (ES) 519 (M⁺).

25 Morpholine-4-carboxylic acid (1-(S)-{1-(S)-[2-(3-benzyloxy-phenyl)-oxazole-5-carbonyl]-3-phenyl-propylcarbamoyl}-3-methyl-butyl)-amide, m.p. 61-3 °C, MS (ES) 639 (M⁺).

Morpholine-4-carboxylic acid {2-cyclohexyl-1-(S)-[1-(R,S)-(4-isobutyl-2-pyrinin-2-yl-oxazole-5-carbonyl)-3-phenyl-propylcarbamoyl]-ethyl} amide, m.p. 93-5 °C, MS (ES) 649 (M⁺).

EXAMPLE 6

5 2-(4-Isobutyloxazol-2-yl)pyridine (Method E)



- 10 *N*-(*t*-Butoxy)-L-leucine (10 g, 43 mmol) was dissolved in 200 mL of CH₂Cl₂. The solution was cooled to 0 °C with an ice-water bath. Carbonyldiimidazole (7.7 g, 47.5 mmol) was added and the reaction mixture was stirred for 1 h. *N,O*-dimethylhydroxylamine hydrochloride (4.64 g, 47.8 mmol) was added at 0 °C. The ice bath was removed and the reaction was stirred at ambient temperature for 16 h. The reaction solution was poured into 200 mL of an ice-cooled solution of 5% citric acid. The organic layer was separated, washed with 2 x 100 mL of 1N HCl, 1 x 100 mL of saturated NaHCO₃, and 2 x 100 mL brine. The organic layer was dried over Na₂SO₄, filtered, and concentrated by rotary evaporation to give [1-(*N*-methoxy-*N*-methylcarbamoyl)-3-methylbutyl]carbamic acid *t*ert-butyl ester as a thick oil (7.39 g, 59% crude) which was used without further purification.

The *t*ert-butyl ester from above (1g, 3.47 mmol) was dissolved in 10 mL CH₂Cl₂ and 5 mL trifluoroacetic acid was added. The reaction mixture was stirred for 1 h. Solvents were evaporated and the residue was taken up in 2 x 10 mL CH₂Cl₂ and evaporated to an

oil. In a separate flask, picolinic acid (470 mg, 3.82 mmol) was dissolved in 10 mL DMF and the resulting solution was cooled to 0 °C. EDC (787 mg, 4.1 mmol) and HOBT (554 mg, 4.1 mmol) were added and the reaction mixture was stirred at 0 °C for 1 h. In a separate flask, the free amine prepared above was dissolved in 5 mL DMF and 1.5 mL N-methylmorpholine was added. This solution was added to the reaction mixture at 0 °C. The reaction mixture was allowed to stir at ambient temperature for 16 h after which time it was poured into a mixture of ice/5% citric acid (100 mL) and extracted with 4 x 30 mL EtOAc. The combined EtOAc extracts were washed with 3 x 100 mL brine, 2 x 100 mL NaHCO₃, 1 x 100 mL brine, dried with Na₂SO₄, and evaporated to an oil which was dried under vacuum yielding 990 mg (100%) of pyridine-2-carboxylic acid [1-(N-methoxy-N-methylcarbamoyl)-3-methylbutyl]amide. This was used without further purification.

The amide from above (4.7 g, 14.7 mmol) was dissolved in 50 mL THF and added to a slurry of LiAlH₄ (558 mg, 14.7 mmol) in 50 mL THF at -78 °C. The reaction mixture was allowed to warm to 0 °C and maintained for 15 min, after which time it was cooled to -78 °C and cannulated into an ice-cooled solution of KHSO₄ (8.16 g, 60 mmol) in 200 mL H₂O. The resulting mixture was extracted with 5 x 100 mL EtOAc. The combined extracts were washed with 2 x 100mL satd.NaHCO₃ and 1 x 100 mL brine, dried with Na₂SO₄ and evaporated to an oily residue which was flash chromatographed through SiO₂ (25% EtOAc/hexane – 35% EtOAc/hexane) yielding 2.8 g (86%) of pyridine-2-carboxylic acid (1-formyl-3-methylbutyl)amide as a colorless oil which solidified on standing.

Hexachloroethane (445 mg, 1.87 mmol) was dissolved in 5 mL CH₃CN. A solution of pyridine-2-carboxylic acid (1-formyl-3-methylbutyl)amide (137.5 mg, 0.625 mmol) in 2 mL CH₃CN was added followed by triethylamine (375 mg, 3.75 mmol) and triphenylphosphine (491 mg, 1.87 mmol). The resulting mixture was stirred for ½ h, poured into brine, and extracted with 2 x 25 mL EtOAc. The combined extracts were washed with 1 x 50 mL brine, dried with Na₂SO₄ and evaporated to 665 mg of a tan solid which was flash chromatographed through SiO₂ (20% - 35% hexane/EtOAc) yielding 100 mg (76%) of the title compound as an amber oil, MS (ES) 203 (M⁺).

ASSESSMENT OF BIOLOGICAL PROPERTIES

5

Expression and Purification of recombinant human Cathepsin S

Cloning of human cathepsin S:

U937 RNA was subjected to reverse transcriptase / polymerase chain reaction with
10 primer A (5'cacaatgaaacggctggttt 3') and primer B (5'ctagattctggtaagaggg 3')
designed to specifically amplify the cathepsin S cDNA. The resulting 900 bp DNA
fragment was subcloned into pGEM-T (Promega) and sequenced to confirm its identity.
This construct was used for all subsequent manipulations. This procedure is typical for
cloning of known genes and is established in its field.

15

Human Pre-Pro-Cat S was removed from pGem-T vector (Promega, 2800 Woods Hollow
Rd, Madison, WI 53711) by digestion with restriction enzyme SacII, followed by
treatment with T4 DNA polymerase to generate a blunt end, and a second restriction
enzyme digest with Sall. It was subcloned into pFastBac1 donor plasmid (GibcoBRL,
20 8717 Grovemont Cr., Gaithersburg, MD 20884) which had been cut with restriction
enzyme BamH1 and blunt-ended and then cut with restriction enzyme Sall. The ligation
mixture was used to transform DH5a competent cells (GibcoBRL) and plated on LB
plates containing 100ug/ml ampicillin. Colonies were grown in overnight cultures of LB
media containing 50ug/ml Ampicillin, plasmid DNA isolated and correct insert
25 confirmed by restriction enzyme digestion. Recombinant pFastBac donor plasmid was
transformed into DH10Bac competent cells (GibcoBRL). Large white colonies were
picked from LB plates containing 50ug/ml kanamycin, 7ug/ml gentamicin, 10ug/ml
tetracycline, 100ug/ml Bluo-gal, and 40ug/ml IPTG. DNA was isolated and used to
transfect Sf9 insect cells using CellFECTIN reagent (GibcoBRL). Cells and supernatant
30 were harvested after 72 hours. Viral supernatant was passaged twice and presence of Cat
S confirmed by PCR of the supernatant.

SF9 cells were infected with recombinant baculovirus at a MOI of 5 for 48-72 hrs. Cell pellet was lysed and incubated in buffer at pH 4.5 at 37 for 2 hours to activate Cat S from pro-form to active mature form (Bromme, D & McGrath, M., *Protein Science*, 1996, 5:789-791.) Presence of Cat S was confirmed by SDS-PAGE and Western blot using 5 rabbit anti-human proCat S.

Inhibition of Cathepsin S

Human recombinant cathepsin S expressed in Baculovirus is used at a final concentration 10 of 10nM in buffer. Buffer is 50mM Na Acetate, pH 6.5, 2.5mMEDTA, 2.5mMTCEP. Enzyme is incubated with either compound or DMSO for 10 min at 37C. Substrate 7-amino-4-methylcoumarin, CBZ-L-valyl-L-valyl-L-arginineamide (custom synthesis by Molecular Probes) is diluted to 20uM in water (final concentration of 5uM), added to assay and incubated for additional 10 minutes at 37 C. Compound activity is measured 15 by diminished fluorescence compared to DMSO control when read at 360nm excitation and 460nm emission.

Examples listed above were evaluated for inhibition of cathepsin S in the above assay.

All had IC₅₀ of 100 micromolar or below.

20 The following prophetic compounds may be made in accordance with the procedure outlined in Scheme IV (Method D), and the specific example 5:

25 Morpholine-4-carboxylic acid {1-[2-(4-isobutyl-2-pyridin-2-yl-oxazol-5-yl)-2-oxo-ethylcarbamoyl]-3-methyl-butyl}-amide;

Morpholine-4-carboxylic acid {1-[2-(4-cyclohexylmethyl-2-pyridin-2-yl-oxazol-5-yl)-2-oxo-ethylcarbamoyl]-3-methyl-butyl}-amide;

30 Morpholine-4-carboxylic acid {1-[2-(4-cyclohexylmethyl-2-pyridin-3-yl-oxazol-5-yl)-2-oxo-ethylcarbamoyl]-3-methyl-butyl}-amide;

Morpholine-4-carboxylic acid {2-cyclohexyl-1-[2-(4-cyclohexylmethyl-2-pyridin-3-yl-oxazol-5-yl)-2-oxo-ethylcarbamoyl]-ethyl}-amide;

- Morpholine-4-carboxylic acid {2-cyclohexyl-1-[2-(4-isobutyl-2-pyridin-3-yl-oxazol-5-yl)-2-oxo-ethylcarbamoyl]-ethyl}-amide;
- 5 Morpholine-4-carboxylic acid {1-[2-(4-isobutyl-2-pyridin-3-yl-oxazol-5-yl)-2-oxo-ethylcarbamoyl]-3-methyl-butyl}-amide;
- Morpholine-4-carboxylic acid {1-[1-(4-isobutyl-2-pyridin-3-yl-oxazole-5-carbonyl)-3-phenyl-propylcarbamoyl]-3-methyl-butyl}-amide;
- 10 Morpholine-4-carboxylic acid {1-[1-(4-isobutyl-2-pyridin-3-yl-oxazole-5-carbonyl)-3-phenyl-propylcarbamoyl]-3,3-dimethyl-butyl}-amide;
- Morpholine-4-carboxylic acid {1-[1-(4-isobutyl-2-pyridin-4-yl-oxazole-5-carbonyl)-3-phenyl-propylcarbamoyl]-3,3-dimethyl-butyl}-amide;
- 15 15 Morpholine-4-carboxylic acid {2-cyclohexyl-1-[1-(4-isobutyl-2-pyridin-4-yl-oxazole-5-carbonyl)-3-phenyl-propylcarbamoyl]-ethyl}-amide;
- Morpholine-4-carboxylic acid {2-cyclohexyl-1-[1-(4-cyclohexylmethyl-2-pyridin-4-yl-oxazole-5-carbonyl)-3-phenyl-propylcarbamoyl]-ethyl}-amide;
- 20 20 Morpholine-4-carboxylic acid (2-cyclohexyl-1-{1-[4-isobutyl-2-(1-methylpiperidin-4-yl)-oxazole-5-carbonyl]-3-phenyl-propylcarbamoyl}-ethyl)-amide;
- Morpholine-4-carboxylic acid (2-cyclohexyl-1-{1-[4-isobutyl-2-(1-methylpiperidin-4-yl)-oxazole-5-carbonyl]-3-phenyl-propylcarbamoyl}-ethyl)-amide;
- 25 25 Morpholine-4-carboxylic acid (1-{1-[4-isobutyl-2-(1-methyl-piperidin-4-yl)-oxazole-5-carbonyl]-3-phenyl-propylcarbamoyl}-3,3-dimethyl-butyl)-amide;
- Morpholine-4-carboxylic acid (1-{1-[4-isobutyl-2-(1-pyrimidin-2-yl-piperidin-4-yl)-oxazole-5-carbonyl]-3-phenyl-propylcarbamoyl}-3,3-dimethyl-butyl)-amide;
- 30 30 Morpholine-4-carboxylic acid (1-{2-[4-isobutyl-2-(1-pyrimidin-2-yl-piperidin-4-yl)-oxazol-5-yl]-2-oxo-ethylcarbamoyl}-3,3-dimethyl-butyl)-amide;
- Morpholine-4-carboxylic acid (1-{2-[4-cyclohexylmethyl-2-(1-pyrimidin-2-yl-piperidin-4-yl)-oxazol-5-yl]-2-oxo-ethylcarbamoyl}-3-methyl-butyl)-amide;
- 35 35 Morpholine-4-carboxylic acid {1-[2-(4-cyclohexylmethyl-2-piperidin-3-yl-oxazol-5-yl)-2-oxo-ethylcarbamoyl]-3-methyl-butyl}-amide;
- Morpholine-4-carboxylic acid {1-[2-(4-cyclohexylmethyl-2-piperidin-3-yl-oxazol-5-yl)-2-oxo-ethylcarbamoyl]-3-methyl-butyl}-amide;
- 40 40 Morpholine-4-carboxylic acid {1-[2-(4-isobutyl-2-piperidin-3-yl-oxazol-5-yl)-2-oxo-ethylcarbamoyl]-3-methyl-butyl}-amide;
- Morpholine-4-carboxylic acid (1-{2-[4-isobutyl-2-(1-methyl-piperidin-3-yl)-oxazol-5-yl]-2-oxo-ethylcarbamoyl}-3-methyl-butyl)-amide;
- 45

- Morpholine-4-carboxylic acid (1-{2-[4-isobutyl-2-(1-methyl-piperidin-3-yl)-oxazol-5-yl]-2-oxo-ethylcarbamoyl}-3,3-dimethyl-butyl)-amide;
- 5 Morpholine-4-carboxylic acid (1-{2-[4-isobutyl-2-(1-methyl-piperidin-2-yl)-oxazol-5-yl]-2-oxo-ethylcarbamoyl}-3,3-dimethyl-butyl)-amide;
- Morpholine-4-carboxylic acid (1-{1-[4-isobutyl-2-(1-methyl-piperidin-2-yl)-oxazole-5-carbonyl]-3-phenyl-propylcarbamoyl}-3-methyl-butyl)-amide;
- 10 Morpholine-4-carboxylic acid {1-[4-isobutyl-2-phenyl-oxazole-5-carbonyl]-3-phenyl-propylcarbamoyl}-3-methyl-butyl)-amide;
- Morpholine-4-carboxylic acid {1-[1-(4-dimethylaminomethyl-2-phenyl-oxazole-5-carbonyl)-3-phenyl-propylcarbamoyl]-3-methyl-butyl}-amide;
- 15 Morpholine-4-carboxylic acid {1-[2-(4-dimethylaminomethyl-2-phenyl-oxazol-5-yl)-2-oxo-ethylcarbamoyl]-3-methyl-butyl}-amide;
- Morpholine-4-carboxylic acid {2-cyclohexyl-1-[2-(4-dimethylaminomethyl-2-phenyl-oxazol-5-yl)-2-oxo-ethylcarbamoyl]-ethyl}-amide;
- 20 Morpholine-4-carboxylic acid {1-[2-(4-dimethylaminomethyl-2-phenyl-oxazol-5-yl)-2-oxo-ethylcarbamoyl]-3,3-dimethyl-butyl}-amide;
- Morpholine-4-carboxylic acid {1-[1-(4-dimethylaminomethyl-2-phenyl-oxazol-5-carbonyl)-3-phenyl-propylcarbamoyl]-3,3-dimethyl-butyl}-amide;
- 25 Morpholine-4-carboxylic acid {1-[1-(4-dimethylaminomethyl-2-phenyl-oxazol-5-carbonyl)-3-phenyl-propylcarbamoyl]-3,3-dimethyl-butyl}-amide;
- Morpholine-4-carboxylic acid {1-[1-(4-hydroxymethyl-2-phenyl-oxazol-5-carbonyl)-3-phenyl-propylcarbamoyl]-3,3-dimethyl-butyl}-amide;
- 30 Morpholine-4-carboxylic acid (3,3-dimethyl-1-{2-[4-(4-methyl-piperazin-1-ylmethyl)-2-phenyl-oxazol-5-yl]-2-oxo-ethylcarbamoyl}-butyl)-amide;
- Morpholine-4-carboxylic acid (3,3-dimethyl-1-{2-[4-(4-methyl-piperazin-1-ylmethyl)-2-pyridin-4-yl-oxazol-5-yl]-2-oxo-ethylcarbamoyl}-butyl)-amide;
- 35 Morpholine-4-carboxylic acid (3-methyl-1-{1-[4-(4-methyl-piperazin-1-ylmethyl)-2-pyridin-4-yl-oxazole-5-carbonyl]-3-phenyl-propylcarbamoyl}-butyl)-amide;
- 40 {1-[4-Isobutyl-5-(2-{4-methyl-2-[(morpholine-4-carbonyl)-amino]-pentoylamino}-acetyl)-oxazol-2-yl]-3-methyl-butyl} carbamic acid benzyl ester;
- Morpholine-4-carboxylic acid {2-cyclohexyl-1-[1-(4-isobutyl-2-pyrimidin-4-yl-oxazole-5-carbonyl)-3-phenyl-propylcarbamoyl]-ethyl}-amide;
- 45

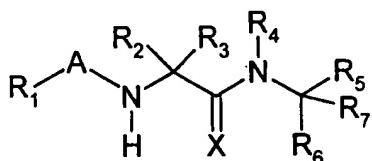
Morpholine-4-carboxylic acid {2-cyclohexyl-1-[3-phenyl-1-(4-phenyl-2-pyridin-4-yl-thiazole-5-carbonyl)-propylcarbamoyl]-ethyl}-amide; and

5 Morpholine-4-carboxylic acid {2-cyclohexyl-1-[2-oxo-2-(2-pyridin-4-yl-4-p-tolyl-thiazole-5-yl)-ethylcarbamoyl]-ethyl}-amide.

Preferred prophetic compounds have S-stereochemistry at their asymmetric carbons.

What is claimed is:

1. A compound of formula (I):



5

(I)

wherein:

10

A is $-C(Y)-$ or $-SO_2-$ Y is O, S or NR_a wherein R_a is selected from the group consisting of H, alkyl, aryl, alkoxy, aryloxy, alkylamino and arylamino;

15

 R_1 is alkyl, cycloalkyl, aryl, heterocycll, heteroaryl or amino wherein R_1 is optionally substituted by one or more R_b ;

20

 R_b is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocycll, heteroaryl, alkoxy, aryloxy, alkoxycarbonyl, aryloxycarbonyl, alkanoyl, aroyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocycll or heteroaryl, alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a

25

sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocycll or heteroaryl, alkoxycarbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl,

30

amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocycll or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R_b may be further optionally substituted by one or more R_c ;

35

 R_c is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocycle, heteroaryl, arylalkyl, alkoxy, aryloxy, arylalkoxy, alkanoyl, aroyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocycll or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

40

R₂ is H or alkyl;

R₃ is H, alkyl, cycloalkyl, aryl, heterocyclyl or heteroaryl, wherein R₃ is optionally substituted by one or more groups of the formula R_d;

5

R_d is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkoxy, aryloxy, arylalkoxy, alkoxycarbonyl, aryloxycarbonyl, alkanoyl, aroyl, alkanoyloxy, aryloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkoxycarbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R_d may be further optionally substituted by one or more R_e;

10

R_e is selected from the group consisting of alkyl, cycloalkyl, aryl, arylalkyl, alkoxy, aryloxy, arylalkoxy, alkanoyl, aroyl, amino, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

15

R₄ is H or alkyl;

R₅ is H, alkyl or cycloalkyl;

20

R₆ is H, alkyl, cycloalkyl, aryl, heterocyclyl or heteroaryl, wherein R₆ is optionally substituted by one or more groups of the formula R_f;

25

R_f is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkoxy, aryloxy, alkanoyl, aroyl, arylalkoxy, heteroarylalkoxy, alkoxycarbonyl, aryloxycarbonyl, alkanoyloxy, aryloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylalkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkoxycarbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono

or di-substituted by alkyl, aryl, heterocycll or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R_f may be further optionally substituted by one or more R_g;

5 R_g is selected from the group consisting of alkyl, cycloalkyl, aryl optionally substituted by halogen, C1-5alkyl or C1-5alkoxy, heterocycll, heteroaryl, alkoxy, aryloxy, arylalkoxy, alkoxycarbonyl, aryloxycarbonyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocycll or
10 heteroaryl; alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocycll or heteroaryl; alkoxycarbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocycll or heteroaryl; halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

20 or R₅ together with R₆ form a 3 to 6 membered carbocyclic ring, the carbocyclic ring being optionally substituted with one or more R_h;

25 R_h is selected from the group consisting of alkyl, aryl, alkoxycarbonyl, aryloxycarbonyl, arylalkoxycarbonyl, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with a group selected from alkyl, cycloalkyl, aryl, arylalkyl, heterocycll or heteroaryl; halogen, hydroxy, carboxy and cyano;

30 R₇ is R₈-C(Z)-;
30 wherein Z is O, S, or NR_i; wherein R_i is selected from the group consisting of H, alkyl, aryl, alkoxy, aryloxy and hydroxy;

35 R₈ is a 5-8 membered monocyclic heteroaryl or 8-11 membered bicyclic heteroaryl ring system, each of the monocyclic or bicyclic ring systems having 1-4 of the same or different heteroatoms selected from the group consisting of N, O and S wherein any of the above R₈ can be optionally substituted by one or more R_j;

40 R_j is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocycll, heteroaryl, arylalkyl, alkoxy, aryloxy, alkanoyl, aroyl, arylalkoxy, alkoxycarbonyl, aryloxycarbonyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocycll or heteroaryl, alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylalkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen

atom may be independently substituted by alkyl, aryl, heterocycl or heteroaryl; alkoxy carbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy, 5 arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocycl or heteroaryl; halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R_j may be further optionally substituted by one or more R_k;

10 R_k is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocycl, heteroaryl, alkoxy, aryloxy, arylalkoxy, alkoxy carbonyl, aryloxycarbonyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocycl or heteroaryl, alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein 15 either nitrogen atom may be independently substituted by alkyl, aryl, heterocycl or heteroaryl, alkoxy carbonylamino, aryloxycarbonylamino, arylalkoxycarbonylamino, arylalkoxycarbonylaminoalkyl, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, 20 arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocycl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

25 X is O, S or N-OH;

and the pharmaceutically acceptable derivatives thereof;

30 with the proviso that when R₆ is alkyl the alkyl must be substituted with R_f wherein R_f is not hydroxy, sulphydryl or halogen.

2. The compound according to claim 1 wherein:

35

R_a is selected from the group consisting of H, alkyl and aryl;

40 R₁ is C1-8 alkyl, C3-7 cycloalkyl, aryl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, pyranyl, thiopyranyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, 45 quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, or amino wherein R₁ is optionally substituted by one or more R_b;

R_b is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkoxy, aryloxy, C1-8 alkoxycarbonyl, aryloxycarbonyl, C1-8 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkanoylamino, aroylamino, C1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoxazinyl, alkoxycarbonylamino, aryloxycarbonylamino, C1-8 alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoxazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R_b may be further optionally substituted by one or more R_c;

R_c is selected from the group consisting of C1-8 alkyl, C3-6 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl;

5 heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkoxy, aryloxy, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

- 10 R₃ is H, C1-8 alkyl, C3-7 cycloalkyl or aryl wherein R₃ is optionally substituted by one or more R_d;
- 15 R_d is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkoxy, aryloxy, alkanoyl, aroyl, C1-8 alkoxycarbonyl, aryloxycarbonyl, C1-8 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl,
- 20 heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkanoylamino, aroylamino, C1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, alkoxycarbonylamino, aryloxycarbonylamino, C1-8 alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl,
- 25
- 30
- 35
- 40
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piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinoliny, isoquinoliny, quinazoliny, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R_d may be further optionally substituted by one or more R_e ;

10 R_c is selected from the group consisting of C1-8 alkyl, C3-6 cycloalkyl, aryl, arylalkyl, C1-8 alkoxy, aryloxy, arylalkoxy, aroyl, amino, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

15 R₅ is H or alkyl;

R_6 is H, C1-8 alkyl, C3-7 cycloalkyl or aryl wherein R_6 is optionally substituted by one or more R_5' .

20 R_f is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkoxy, aryloxy, arylC1-8alkoxy, heteroarylC1-8alkoxy, C1-8 alkoxycarbonyl, aryloxycarbonyl, C1-8 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkanoylamino, aroylamino, C1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylC1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl,

pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl,
benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl,
quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoaxazinyl,
alkoxycarbonylamino, aryloxycarbonylamino, C1-8 alkylcarbamoyloxy,
5 arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl,
arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono
or di-substituted by alkyl, aryl, heterocycl selected from the group consisting of
pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl
10 or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl,
oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl,
tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl,
isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl,
15 benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl,
carbazolyl, phenothiazinyl and phenoaxazinyl, halogen, hydroxy, oxo, carboxy,
cyano, nitro, amidino and guanidino, R_f may be further optionally substituted by
one or more R_g;

R_g is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl,
20 aryl optionally substituted by halogen, C1-3alkyl or C1-3alkoxy;
heterocycl selected from the group consisting of pyrrolidinyl,
piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl;
heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl,
oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl,
25 triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl,
pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl,
benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl,
quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoaxazinyl,
C1-8 alkoxy, aryloxy, arylC1-8alkoxy, C1-8 alkoxycarbonyl,
aryloxycarbonyl, C1-8 alkanoyloxy, aroyloxy, carbamoyl wherein the
30 nitrogen atom may be independently mono or di-substituted by C1-8 alkyl,
aryl, heterocycl selected from the group consisting of pyrrolidinyl,
piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or
heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl,
oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl,
35 triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl,
pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl,
benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl,
quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoaxazinyl,
C1-8 alkanoylamino, aroylamino, C1-8 alkylthio wherein the sulfur atom
40 may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom
may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen
atom may be independently substituted by alkyl, aryl, heterocycl
selected from the group consisting of pyrrolidinyl, piperidinyl,
morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl
45 selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,
thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl,

- tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl,
 5 indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl,
 benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl,
 10 quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl or phenoazinyl,
 alkoxy carbonylamino, aryloxy carbonylamino, C1-8 alkylcarbamoyloxy,
 arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino,
 alkylaminosulfonyl and arylaminosulfonyl, amino wherein the nitrogen
 15 atom may be independently mono or di-substituted by alkyl, aryl,
 heterocycl selected from the group consisting of pyrrolidinyl,
 piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or
 heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl,
 20 oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl,
 triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl,
 pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl,
 25 benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl,
 quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoazinyl,
 halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;
- R_h is selected from the group consisting of C1-8 alkyl, aryl, C1-8 alkoxy carbonyl,
 30 aryloxy carbonyl, arylC1-8alkoxy carbonyl, carbamoyl wherein the nitrogen atom
 may be optionally mono or di-substituted with a group selected from C1-8 alkyl,
 C3-7 cycloalkyl, aryl, arylC1-8alkyl, heterocycl selected from the group
 35 consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl
 and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl,
 pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl,
 triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl,
 40 indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl,
 benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny,
 carbazolyl, phenothiazinyl and phenoazinyl, halogen, hydroxy, carboxy and
 cyano;
- R_g is a heteroaryl ring selected from the group consisting of furanyl, thienyl, pyrrolyl,
 45 oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, pyridyl, pyridazinyl,
 pyrimidinyl, pyrazinyl, triazinyl, indolizinyl, indolyl, isoindolyl, benzofuranyl,
 benzothienyl, indazolyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, triazolyl,
 tetrazolyl, purinyl, quinolizinyl, quinolinyl, isoquinolinyl, cinnolinyl, phthalazinyl,
 quinazolinyl, quinoxaliny, naphthyridinyl, pteridinyl, carbazolyl, acridinyl and
 phenazinyl, wherein any of the above R_g can be optionally substituted by one or more R_j;
- R_j is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocycl
 50 selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl,
 thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group
 consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl,

isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl,
 5 pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl,
 benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl,
 quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoazinyl,
 arylalkyl, alkoxy, aryloxy, arylalkoxy, alkoxy carbonyl, aryloxycarbonyl,
 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be
 independently mono or di-substituted by alkyl, aryl, heterocycl selected from
 10 the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl,
 piperazinyl and indolinyl, or heteroaryl selected from the group consisting of
 furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl,
 oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl,
 15 pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl,
 benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl,
 quinoxaliny, carbazolyl, phenothiazinyl and phenoazinyl, alkanoylamino,
 aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or
 sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or
 sulfone, arylalkylthio wherein the sulfur atom may be oxidized to a sulfoxide or
 sulfone, ureido wherein either nitrogen atom may be independently substituted by
 20 alkyl, aryl, heterocycl selected from the group consisting of pyrrolidinyl,
 piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl
 selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,
 thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl,
 thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl,
 25 benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl,
 quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl
 and phenoazinyl, alkoxy carbonylamino, aryloxycarbonylamino, C1-8
 alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino,
 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be
 30 independently mono or di-substituted by alkyl, aryl, heterocycl selected from
 the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl,
 piperazinyl and indolinyl, or heteroaryl selected from the group consisting of
 furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl,
 oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl,
 35 pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl,
 benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl,
 quinoxaliny, carbazolyl, phenothiazinyl and phenoazinyl, halogen, hydroxy,
 oxo, carboxy, cyano, nitro, amidino and guanidino, R_j may be further optionally
 substituted by one or more R_k;

40 R_k is selected from the group consisting of alkyl, cycloalkyl, aryl,
 heterocycl selected from the group consisting of pyrrolidinyl,
 piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl;
 heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl,
 oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl,
 45 triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl,
 pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl,

benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl,
quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoazinyl,
alkoxy, aryloxy, arylalkoxy, alkoxy carbonyl, aryloxycarbonyl,
alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be
5 independently mono or di-substituted by alkyl, aryl, heterocycl selected
from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl,
thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the
group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl,
10 imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl,
thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl,
isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl,
benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl,
quinoxalinyl, carbazolyl, phenothiazinyl and phenoazinyl,
15 alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be
oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be
oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom
may be independently substituted by alkyl, aryl, heterocycl selected
from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl,
20 thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the
group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl,
imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl,
thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl,
isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl,
benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl,
25 quinoxalinyl, carbazolyl, phenothiazinyl and phenoazinyl,
alkoxycarbonylamino, aryloxycarbonylamino, arylalkoxycarbonylamino,
arylalkoxycarbonylaminoalkyl, C1-8 alkylcarbamoyloxy,
arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino,
alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom
30 may be independently mono or di-substituted by alkyl, aryl, heterocycl
selected from the group consisting of pyrrolidinyl, piperidinyl,
morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl
selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,
thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl,
35 tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl,
indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl,
benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl,
quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoazinyl,
halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;
40

and X is O or S.

45 3. The compound according to claim 2 wherein:

Y is O or S;

- 5 R₁ is C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, pyranlyl, thiopyranlyl, piperazinyl and indolinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, 10 benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny or amino wherein R₁ is optionally substituted by one or more R_b;

R_b is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, 15 piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, 20 quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny, C1-5 alkoxy, aryloxy, C1-5 alkoxy carbonyl, aryloxy carbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, 25 thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of 30 pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, 35 quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny, C1-5 alkoxy carbonylamino, aryloxy carbonylamino, C1-5 alkyl carbamoyloxy, aryl carbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, 40 quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny, C1-5 alkyl carbamoyloxy, aryl carbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, 45 quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny, halogen, hydroxy, oxo, carboxy, cyano, nitro,

amidino and guanidino, R_b may be further optionally substituted by one or more R_c;

R_c is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl, 5 aryl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl and pyridinyl, C1-5 alkoxy, aryloxy, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

10 R₂ is H or C1-3 alkyl;

R₃ is H, C1-5 alkyl, C3-7 cycloalkyl or aryl, wherein R₃ is optionally substituted by one or more R_d;

15 R_d is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, 20 benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxy, aryloxy, C1-5alkanoyl, aroyl, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di- 25 substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur 30 atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 35 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected 40 from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, 45

imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R_d may be further optionally substituted by one or more R_e;

5

R_e is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl, aryl, arylalkyl, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, aroyl, amino, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

10

R₄ is H or C1-3 alkyl;

15

R₅ is H or C1-8 alkyl;

20 R₆ is H, C1-5 alkyl, C3-7 cycloalkyl or aryl wherein R₆ is optionally substituted by one or more R_f;

25

R_f is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, aryl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, heteroarylC1-5alkoxy, C1-5 alkoxy carbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylC1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl,

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quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5
alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy,
arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5
alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be
5 independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected
from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl,
thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group
10 consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl,
tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl,
benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl,
quinazolinyl and quinoxalinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro,
amidino and guanidino, R_f may be further optionally substituted by one or more
R_g;

15 R_g is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl,
aryl optionally substituted by halogen, methyl or methoxy; heterocyclyl
selected from the group consisting of pyrrolidinyl, piperidinyl,
morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl
selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,
20 thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl,
pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl,
benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and
quinoxalinyl, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, C1-5
alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl
25 wherein the nitrogen atom may be independently mono or di-substituted
by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of
pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and
indolinyl or heteroaryl selected from the group consisting of furanyl,
thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl,
30 pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl,
benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl,
quinazolinyl and quinoxalinyl, C1-5 alkanoylamino, aroylamino, C1-5
alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or
sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or
35 sulfone, ureido wherein either nitrogen atom may be independently
substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group
consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl,
piperazinyl and indolinyl, or heteroaryl selected from the group consisting
of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl,
40 tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl,
benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl,
isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxycarbonylamino,
aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5
alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl,
45 arylaminosulfonyl, amino wherein the nitrogen atom may be
independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl

selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

10

R_b is selected from the group consisting of C1-5 alkyl, aryl, C1-5 alkoxycarbonyl, aryloxycarbonyl, arylC1-5alkoxycarbonyl, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with a group selected from C1-5 alkyl, C3-7 cycloalkyl, aryl, arylC1-5alkyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, halogen, hydroxy, carboxy and cyano;

R_i is alkoxy, aryloxy or hydroxy;

25

R₈ is a heteroaryl ring selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, indolizinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, indazolyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolizinyl, quinolinyl, isoquinolinyl, cinnolinyl, phthalazinyl, quinazolinyl, quinoxalinyl, naphthyridinyl, pteridinyl, carbazolyl, acridinyl and phenazinyl, wherein any of the above R₈ can be optionally substituted by one or more R_j;

35

R_j is selected from the group consisting of C1-8alkyl, C3-7cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl; arylC1-8alkyl, C1-8alkoxy, aryloxy, arylC1-8alkoxy, C1-8alkoxycarbonyl, aryloxycarbonyl, C1-8alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl

selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8alkanoylamino, aroylamino, C1-8alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylC1-8alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, carbazolyl, phenothiazinyl and phenoxazinyl, alkoxy carbonylamino, aryloxy carbonylamino, C1-8 alkyl carbamoyloxy, aryl carbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoxazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R_j may be further optionally substituted by one or more R_k;

R_k is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkoxy, aryloxy, arylC1-8alkoxy, C1-8alkoxy carbonyl, aryloxy carbonyl, C1-8alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl,

oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl,
 triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl,
 pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl,
 benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl,
 5 quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl,
 alkanoylamino, aroylamino, C1-8alkylthio wherein the sulfur atom may be
 oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be
 oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom
 10 may be independently substituted by C1-8alkyl, aryl, heterocyclyl selected
 from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl,
 thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the
 group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl,
 imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl,
 15 thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl,
 isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl,
 benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl,
 quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-
 8alkoxycarbonylamino, aryloxycarbonylamino, arylC1-
 20 8alkoxycarbonylamino, arylalkoxycarbonylaminoC1-8alkyl, C1-8
 alkylcarbamoyloxy, arylcarbamoyloxy, C1-8alkylsulfonylamino,
 arylsulfonylamino, C1-8alkylaminosulfonyl, arylaminosulfonyl, amino
 wherein the nitrogen atom may be independently mono or di-substituted
 25 by C1-8alkyl, aryl, heterocyclyl selected from the group consisting of
 pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and
 indolinyl, or heteroaryl selected from the group consisting of furanyl,
 thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl,
 oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl,
 30 pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl,
 benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl,
 isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and
 phenoxazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and
 guanidino.

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4. The compound according to claim 3 wherein:

Y is O;

40 R₁ is C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group
 consisting of piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, pyranyl and
 thiopyranyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl,
 oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl,
 benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, or amino
 45 wherein R₁ is optionally substituted by one or more R_b;

R_b is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl; C1-5 alkoxy, aryloxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl or aryl; C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy, cyano and nitro, R_b may be further optionally substituted by one or more R_c;

R_c is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl, aryl, C1-5 alkoxy, aryloxy, halogen, hydroxy, oxo, carboxy, and cyano;

R₂ is H or methyl;

R₃ is H, C1-5 alkyl, C3-7 cycloalkyl or phenyl, wherein R₃ is optionally substituted by one or more R_d;

R_d is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5 alkoxy, aryloxy, aroyl, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of

furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio
5 wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5 alkoxy carbonylamino, aryloxy carbonylamino, C1-5 alkyl carbamoyloxy, aryl carbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein
10 the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy and cyano, R_d may
15 wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy and cyano, R_d may
20 be further optionally substituted by one or more R_e;

25 R_e is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl, aryl, arylC1-5alkyl, C1-5 alkoxy, aryloxy, arylC1-3alkoxy, aroyl, amino, halogen, hydroxy, oxo, carboxy and cyano;

30 R₄ is H or methyl;

35 R₅ is H or C1-5 alkyl;

R₆ is H, C1-5 alkyl, C3-7 cycloalkyl, phenyl or naphthyl wherein R₆ is optionally substituted by one or more R_f;

40 R_f is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, pyridylC1-5alkoxy, thienylC1-5alkoxy, furanylC1-5alkoxy, C1-5
45 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5

alkyl, aryl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylC1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy and cyano, Rf may be further optionally substituted by one or more R_g,

R_g is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, phenyl optionally substituted by halogen, methyl or methoxy; naphthyl optionally substituted by halogen, methyl or methoxy; heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indoliny; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and

- 5 piperazinyl or heteroaryl selected from the group consisting of furanyl, thieryl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, C1-5 alkoxy carbonylamino, aryloxycarbonylamino, C1-5 alkyl carbamoyloxy, aryl carbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thieryl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy and cyano;
- 10 R_h is selected from the group consisting of C1-5 alkyl, phenyl, naphthyl, C1-5 alkoxy carbonyl, aryloxycarbonyl, arylC1-3alkoxy carbonyl, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with a group selected from C1-5 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, arylC1-3alkyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thieryl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, carboxy and cyano;
- 15 30 Z is O or S;
- 20 R_g is a heteroaryl ring selected from the group consisting of furanyl, thieryl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, indolizinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, indazolyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolizinyl, quinolinyl, isoquinolinyl, cinnolinyl, phthalazinyl, quinazolinyl, quinoxalinyl, naphthyridinyl, pteridinyl, carbazolyl, acridinyl and phenazinyl, wherein any of the above R_g can be optionally substituted by one or more groups of the formula R_j;
- 25 35 40 R_j is selected from the group consisting of C1-5alkyl, C3-6cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thieryl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, arylC1-5alkyl, C1-5alkoxy, aryloxy, arylC1-

Salkoxy, C1-Salkoxycarbonyl, aryloxycarbonyl, C1-Salkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-Salkyl, aryl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-Salkanoylamino, aroylamino, C1-Salkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylC1-Salkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-Salkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-Salkylsulfonylamino, arylsulfonylamino, C1-Salkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, Rj may be further optionally substituted by one or more Rk;

30 R_k is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, tetrazolyl and pyridinyl, C1-3 alkoxy, aryloxy, arylC1-3alkoxy, C1-3alkoxycarbonyl, aryloxycarbonyl, C1-3alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, aryl, heterocyclyl
35 selected from the group consisting of morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, and pyridinyl, C1-3alkanoylamino, aroylamino, C1-3alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-3alkyl, phenyl, naphthyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl and pyridinyl, C1-3alkoxycarbonylamino, aryloxycarbonylamino, arylC1-45 3alkoxycarbonylamino, benzylloxycarbonylaminoC1-5alkyl, C1-3alkylcarbamoyloxy, arylcarbamoyloxy, C1-3alkylsulfonylamino,

arylsulfonylamino, C1-3alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3alkyl, aryl, heterocycl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolylpyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy, cyano and nitro;

10 and

X is O.

15

5. The compound according to claim 4 wherein:

20 R₁ is C1-5 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocycl selected from the group consisting of piperidinyl, morpholinyl, piperazinyl, pyranyl and thiopyranyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, or amino, wherein R₁ is optionally substituted by one or more R_b;

25

30 R_b is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-3 alkoxy, phenoxy, C1-3 alkoxy carbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5alkyl, phenyl or naphthyl; C1-5 alkoxy carbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5alkyl, phenyl, naphthyl, heterocycl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,

thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy and cyano, R_b may be further optionally substituted by one or more R_c;

5

R_c is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, aryl, C1-3 alkoxy, phenoxy, halogen, hydroxy, oxo, carboxy and cyano;

R₂ is H;

10

R₃ is C1-5 alkyl, C3-6 cycloalkyl or phenyl, wherein R₃ is optionally substituted by one or more R_d;

15

R_d is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, quinolinyl and isoquinolinyl, C1-5 alkoxy, phenoxy, aroyl, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, C1-5 alkanoylamino, aroylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, phenylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-3 alkyl, phenyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, C1-5 alkoxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, phenyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, halogen, hydroxy, oxo, carboxy and cyano, R_d may be further optionally substituted by one or more R_e;

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R_e is selected from the group consisting of C1-5 alkyl, C5-6 cycloalkyl, phenyl, naphthyl, arylC1-3alkyl, C1-5 alkoxy, phenoxy, arylC1-3alkoxy, aroyl, amino, halogen, hydroxy, oxo, carboxy and cyano;

wherein the configuration at the stereocenter defined by R₂ and R₃ and the carbon they are attached to is L;

45

R₄ is H;

R₅ is H or C1-3 alkyl;

5

R₆ is H, C1-5 alkyl, C3-6 cycloalkyl or phenyl. wherein R₆ is optionally substituted by one or more R_f;

10 R_f is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5 alkoxy, aryloxy, arylC1-3alkoxy, pyridylC1-5alkoxy, thienylC1-5alkoxy, furanylC1-5alkoxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, C1-5 alkanoylamino, aroylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylC1-3alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl or phenyl; C1-5 alkoxycarbonylamino, C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, halogen, hydroxy, oxo, carboxy and cyano, R_f may be further optionally substituted by one or more R_g;

35 R_g is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl optionally substituted by halogen, methyl or methoxy; heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, pyrimidinyl, pyrazinyl and indolyl, C1-5 alkoxy, aryloxy, arylC1-3alkoxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or aryl; C1-5 alkanoylamino, aroylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl or aryl; C1-5

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5 alkoxy carbonylamino, aryloxy carbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or aryl; halogen, hydroxy, oxo, carboxy and cyano;

10 R_h is selected from the group consisting of C1-5 alkyl, phenyl, C1-5 alkoxy carbonyl, aryloxy carbonyl, arylC1-3alkoxy carbonyl, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with C1-5 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, arylC1-3alkyl, halogen, hydroxy, carboxy and cyano;

15 15 wherein Z is O;

20 R_g is a heteroaryl ring selected from the group consisting of oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, wherein any of the above R_g can be optionally substituted by one or more R_j;

25 R_j is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl, naphthyl, morpholinyl, piperazinyl, furanyl, thienyl, pyrrolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, arylC1-3alkyl, C1-3alkoxy, aryloxy, arylC1-3alkoxy, C1-3alkoxycarbonyl, aryloxy carbonyl, C1-3alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3alkyl, phenyl, naphthyl, piperidinyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl or isoquinolinyl; C1-3alkanoylamino, aroylamino, C1-3alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylC1-3alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-3 alkyl, phenyl, naphthyl, piperidinyl, morpholinyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl or isoquinolinyl; C1-3 alkoxy carbonylamino, aryloxy carbonylamino, C1-3 alkylcarbamoyloxy, arylcarbamoyloxy, C1-3alkylsulfonylamino, arylsulfonylamino, C1-3alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, phenyl, naphthyl, piperidinyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl,

benzoxazolyl, quinolinyl or isoquinolinyl; halogen, hydroxy, oxo, carboxy, cyano and nitro, R_j may be further optionally substituted by one or more R_k;

R_k is selected from the group consisting of methyl, C5-6 cycloalkyl,
5 phenyl, morpholinyl, furanyl, thienyl, pyrrolyl, tetrazolyl, pyridinyl, methoxy, phenoxy, benzyloxy, methoxycarbonyl, acetyloxy, benzoyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-
10 substituted by C1-3 alkyl, phenyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl or pyridinyl; acetyl amino, benzoyl amino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by methyl, phenyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl or
15 pyridinyl; arylC1-3alkoxycarbonylamino, benzoxycarbonylaminoC1-5alkyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3alkyl, phenyl, naphthyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl or isoquinolinyl, halogen, hydroxy, oxo, carboxy, cyano and nitro.

20

6. The compound according to claim 5 wherein:

R₁ is C1-3 alkyl, C5-6 cycloalkyl, phenyl, naphthyl, heterocycl selected from the group consisting of piperidinyl, morpholinyl, piperazinyl, pyranyl and thiopyranyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, or amino, wherein R₁ is optionally substituted by one or more R_b;

R_b is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl, heterocycl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-3 alkoxy, C1-3 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-
35 substituted by C1-3 alkyl, phenyl or heteroaryl selected from the group consisting of pyrrolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-3 alkoxy, C1-3 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-
40 substituted by C1-3 alkyl, phenyl or heteroaryl selected from the group consisting of pyrrolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl and benzthiazolyl; C1-5 alkanoyl amino, aroyl amino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-3alkyl or phenyl; C1-5 alkylsulfonyl amino, arylsulfonyl amino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3alkyl, phenyl,
45

- 5 heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of pyrrolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl; halogen, hydroxy, oxo, carboxy and cyano, R_b may be further optionally substituted by one or more R_c;
- 10 R_c is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, C1-3 alkoxy, halogen and hydroxy;
- 15 10 R₃ is C1-5 alkyl, C5-6 cycloalkyl or phenyl wherein R₃ is optionally substituted by one or more R_d;
- 15 R_d is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, 4-piperidinyl, 4-morpholinyl, piperazinyl, furanyl, thieryl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-5 alkoxy, phenoxy, aroyl, C1-5 alkoxy carbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or phenyl; C1-5 alkanoylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-3 alkyl or phenyl; C1-5 alkoxy carbonylamino, C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; halogen, hydroxy, oxo, carboxy and cyano, R_d may be further optionally substituted by one or more R_e;
- 20 25 R_e is selected from the group consisting of C1-5 alkyl, C5-6 cycloalkyl, phenyl, benzyl, C1-5 alkoxy, phenoxy, benzyloxy, aroyl, halogen, hydroxy, oxo, carboxy and cyano;
- 20 30 R₆ is H, C1-5 alkyl or phenyl wherein R₆ is optionally substituted by one or more R_f;
- 25 35 R_f is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, furanyl, thieryl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-3 alkoxy, benzyloxy, pyridyl, C1-3 alkoxy, thierylC1-3 alkoxy, furanylC1-3 alkoxy, C1-3 alkoxy carbonyl, phenoxy carbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; C1-5 alkanoylamino, aroylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl or phenyl; C1-3 alkoxy carbonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or phenyl; halogen, hydroxy, oxo, carboxy and cyano, R_f may be further optionally substituted by one or more R_g;

- 5 R_g is selected from the group consisting of C1-3 alkyl, phenyl optionally substituted by halogen, methyl or methoxy; heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl and
10 pyridinyl, C1-3 alkoxy, aryloxy, benzyloxy, C1-5 alkoxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or phenyl; C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl or phenyl; C1-5
15 alkoxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-3 alkylsulfonylamino, arylsulfonylamino, C1-3 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; halogen, hydroxy, oxo, carboxy and cyano;
- 20 R_h is selected from the group consisting of C1-3 alkyl, phenyl, C1-3 alkoxycarbonyl, phenoxyoxycarbonyl, benzyloxy, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with C1-5 alkyl, phenyl, benzyl, halogen, hydroxy, carboxy and cyano;
- 25 R_g is a heteroaryl ring selected from the group consisting of oxazolyl, thiazolyl, imidazolyl, pyridyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, wherein any of the above R_g can be optionally substituted by one or more R_j;
- 30 R_j is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl, naphthyl, morpholinyl, piperazinyl, furanyl, thienyl, pyrrolyl, tetrazolyl, pyridinyl, benzyl, C1-3alkoxy, phenoxy, benzyloxy, C1-3alkoxycarbonyl, acetyloxy, benzoyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by methyl, phenyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl or pyridinyl; acetylarnino, benzoylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by methyl, phenyl, thiazolyl, imidazolyl or pyridinyl; C1-3 alkoxycarbonylamino, C1-3 alkylcarbamoyloxy, arylcarbamoyloxy, C1-3alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by methyl, phenyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl or pyridinyl; halogen, hydroxy, carboxy, cyano and nitro, R_j may be further optionally substituted by one or more R_k;
- 45

R_k is selected from the group consisting of methyl, C5-6 cycloalkyl, phenyl, furanyl, thienyl, pyrrolyl, pyridinyl, methoxy, phenoxy, benzyloxy, methoxycarbonyl, acyloxy, benzoxyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by methyl, phenyl, furanyl or thienyl; acetyl amino, benzoyl amino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by methyl, phenyl, furanyl, thienyl, pyrrolyl, oxazolyl and thiazolyl, benzyloxycarbonylamino, benzyloxycarbonylaminoC1-5alkyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3alkyl, phenyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl and pyridinyl, halogen, hydroxy, carboxy, cyano and nitro.

15

7. The compound according to claim 6 wherein:

20

R₁ is C5-6 cycloalkyl, phenyl, naphthyl, piperidinyl, morpholinyl, piperazinyl, furanyl, thienyl, pyrrolyl, pyranyl, thiopyranyl or amino wherein R₁ is optionally substituted by one or more R_b;

25

R_b is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl, furanyl, thienyl, pyrrolyl, imidazolyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, C1-3 alkoxy, C1-3 alkoxy carbonyl, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; C1-5 alkanoyl amino, aroyl amino, ureido wherein either nitrogen atom may be independently substituted by C1-3alkyl or phenyl; C1-5 alkylsulfonyl amino, arylsulfonyl amino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3alkyl or phenyl;, halogen, hydroxy, oxo, carboxy and cyano, R_b may be further optionally substituted by one or more R_c;

35

R_c is selected from the group consisting of C1-3 alkyl, C1-3 alkoxy, halogen and hydroxy;

40

R_d is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, 4-piperidinyl, furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-3alkoxy, C1-5alkoxycarbonyl, C1-5alkanoyloxy, benzoxyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3alkyl or phenyl; C1-5alkanoyl amino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, C1-3alkoxycarbonylamino, C1-3alkylsulfonyl amino, amino wherein the nitrogen atom may be independently

mono or di-substituted by C1-3 alkyl or phenyl, halogen, hydroxy, oxo, carboxy and cyano, R_d may be further optionally substituted by one or more R_e;

5 R_e is selected from the group consisting of C1-3 alkyl, phenyl, benzyl, C1-3 alkoxy, phenoxy, benzyloxy, benzoyl, halogen, hydroxy, oxo, carboxy and cyano;

R_f is H or methyl;

10 R₆ is C1-5 alkyl or phenyl, wherein R₆ is optionally substituted by one or more groups of the formula R_f,

15 R_f is selected from the group consisting of methyl, C3-6 cycloalkyl, phenyl, naphthyl, furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-3 alkoxy, benzyloxy, C1-5 alkanoylamino, aroylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, C1-3 alkoxy carbonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5
20 alkyl or phenyl; halogen, hydroxy, oxo, carboxy and cyano, R_f may be further optionally substituted by one or more R_g;

25 R_g is selected from the group consisting of C1-3 alkyl, phenyl optionally substituted by halogen or methyl; C1-3 alkoxy, aryloxy, benzyloxy, C1-3 alkoxy carbonyl, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; C1-5 alkanoylamino, aroylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; halogen, hydroxy, oxo, carboxy and cyano;

30

R_h is selected from the group consisting of C1-3 alkyl, phenyl, C1-3 alkoxy carbonyl, benzyloxy and carboxy;

35

R₈ is a heteroaryl ring selected from the group consisting of oxazolyl, thiazolyl, imidazolyl, pyridyl, benzimidazolyl, benzothiazolyl and benzoxazolyl, wherein any of the above R₈ can be optionally substituted by one or more R_j;

40

R_j is selected from the group consisting of methyl, cyclohexyl, phenyl, furanyl, thienyl, benzyl, methoxy, phenoxy, benzyloxy, methoxycarbonyl, acetyloxy, benzyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by methyl, phenyl, furanyl or thienyl; acetyl amino, benzoylamino, ureido wherein either nitrogen atom may be independently substituted by methyl or phenyl; methoxycarbonylamino, C1-3 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by

methyl, phenyl, furanyl or thienyl; halogen, hydroxy, carboxy and cyano, R_j may be further optionally substituted by one or more R_k;

5 R_k is selected from the group consisting of methyl, phenyl, furanyl, thienyl, methoxy, phenoxy, benzyloxy, methoxycarbonyl, acetyloxy, benzoyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by methyl or phenyl; acetyl amino, benzoyl amino, ureido wherein either nitrogen atom may be independently substituted by methyl or phenyl; benzyloxycarbonyl amino, benzyloxycarbonyl amino C1-10 3alkyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3alkyl, phenyl, furanyl or thienyl; halogen, hydroxy, carboxy, cyano and nitro.

15

8. The compound according to claim 7 wherein:

A is -C(O)- or -SO₂-;

20

R₁ is cyclohexyl, phenyl, naphthyl, piperidinyl, morpholinyl, piperazinyl, pyranyl, thiopyranyl or amino, wherein R₁ is optionally substituted by one or more R_b;

25 R_b is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl, furanyl, thienyl, pyrrolyl, imidazolyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, C1-3 alkoxy, C1-3 alkoxy carbonyl, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; C1-5 alkanoyl amino, aroyl amino, C1-5 30 alkylsulfonyl amino, arylsulfonyl amino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl; halogen, hydroxy, oxo, carboxy and cyano, R_b may be further optionally substituted by one or more R_c;

35

R_c is selected from the group consisting of C1-3 alkoxy, halogen and hydroxy;

R₃ is C1-5 alkyl or C5-6 cycloalkyl, wherein R₃ is optionally substituted by one or more R_d;

40

R_d is selected from the group consisting of methyl, C3-6 cycloalkyl, phenyl, thienyl, imidazolyl, pyridinyl, indolyl, C1-4 alkoxy, C1-5 alkanoyl amino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, halogen, hydroxy, oxo, carboxy and cyano, R_d may be further optionally substituted by one or more R_e;

45

R_c is selected from the group consisting of methyl, phenyl, benzyl, methoxy, phenoxy, benzyloxy, benzoyl, halogen and hydroxy;

5 R_f is selected from the group consisting of C3-6 cycloalkyl, phenyl, naphthyl, thiaryl, imidazolyl, pyridinyl, indolyl, methoxy, benzyloxy, C1-3 alkanoylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, methoxycarbonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl; halogen, hydroxy, carboxy and cyano, R_f may be further optionally substituted by one or more R_g;

10 R_g is selected from the group consisting of methyl, phenyl optionally substituted by halogen or methyl; methoxy, phenoxy, benzyloxy, methoxycarbonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; halogen, hydroxy and carboxy;

15 R_g is a heteroaryl ring selected from the group consisting of oxazolyl, thiazolyl, imidazolyl, pyridyl, benzthiazolyl and benzoxazolyl, wherein any of the above R_g can be optionally substituted by one or more R_j;

20 R_j is selected from the group consisting of methyl, phenyl, furanyl, thieryl, benzyl, methoxy, methoxycarbonyl, acetyloxy, benzyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by methyl or phenyl; acetylarnino, benzoylarnino, ureido wherein either nitrogen atom may be independently substituted by methyl or phenyl; methoxycarbonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by methyl or phenyl; halogen, hydroxy, carboxy and cyano, R_j may be further optionally substituted by one or more R_k;

25 R_k is selected from the group consisting of methyl, phenyl, methoxy, phenoxy, benzyloxy, methoxycarbonyl, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by methyl or phenyl; ureido wherein either nitrogen atom may be independently substituted by methyl or phenyl; benzyloxycarbonylamino, benzyloxycarbonylaminoC1-5alkyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3alkyl, phenyl, furanyl or thieryl; halogen, hydroxy, carboxy, cyano and nitro.

30

35 9. The compound according to claim 8 wherein:

40

45

R₁ is cyclohexyl, phenyl, naphthyl, piperidinyl, morpholinyl, piperazinyl, pyranyl or thiopyranyl, wherein R₁ is optionally substituted by one or more R_b;

5 R_b is selected from the group consisting of, pyrrolyl, imidazolyl, indolyl, benzimidazolyl, methoxy, methoxycarbonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl; halogen, hydroxy and carboxy, R_b may be further optionally substituted by one or more R_c;

10 R_c is selected from the group consisting of methoxy, halogen and hydroxy;

15 R_d is selected from the group consisting of methyl, C3-6 cycloalkyl, phenyl, C1-4 alkoxy, C1-3 alkanoylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, halogen, hydroxy, oxo, carboxy and cyano, R_d may be further optionally substituted by one or more R_e;

R_e is selected from the group consisting of methyl, phenyl, methoxy, halogen and hydroxy;

20 R_f is H;

25 R_f is selected from the group consisting of C5-6 cycloalkyl, phenyl, naphthyl, thienyl, indolyl, methoxy, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, methoxycarbonylamino, halogen, hydroxy, carboxy and cyano, R_f may be further optionally substituted by one or more R_g;

30 R_g is selected from the group consisting of methyl, phenyl optionally substituted by halogen; methoxy, phenoxy, benzyloxy, methoxycarbonyl, halogen, hydroxy and carboxy;

35

R_g is a heteroaryl ring selected from the group consisting of oxazolyl, pyridyl, benzthiazolyl and benzoxazolyl, wherein any of the above R_g can be optionally substituted by one or more R_j;

40

R_j is selected from the group consisting of methyl, phenyl, benzyl, methoxy, methoxycarbonyl, acetyloxy, benzyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by methyl or phenyl; methoxycarbonylamino, halogen, hydroxy and carboxy, R_j may be further optionally substituted by one or more R_k;

45

R_k is selected from the group consisting of methyl, phenyl, methoxy, methoxycarbonyl, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by methyl or phenyl; benzyloxycarbonylamino, amino wherein the nitrogen atom may be

independently mono or di-substituted by methyl or phenyl; halogen, hydroxy and carboxy.

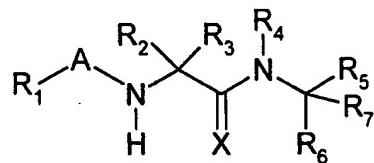
5

10. The compound according to claim 9 wherein:

- 10 R₁ is phenyl or 4-morpholinyl, wherein R₁ is optionally substituted by one or more R_b;
R_b is selected from the group consisting of benzimidazolyl, methoxy and dimethylamino, R_b may be further optionally substituted by a halogen atom;
- 15 R₃ is C1-5 alkyl wherein R₃ is optionally substituted by one or more R_d;
R_d is selected from the group consisting of C3-6 cycloalkyl and phenyl, R_d may be further optionally substituted by one or more R_e;
20 R_e is selected from the group consisting of methyl and halogen;
R₆ is C1-5 alkyl optionally substituted by one or more R_f;
25 R_f is selected from the group consisting of C5-6 cycloalkyl, phenyl, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, and halogen, R_f may be further optionally substituted by one or more R_g;
R_g is selected from the group consisting of methyl, methoxy, methoxycarbonyl, halogen and hydroxy;
- 30 R₈ is a heteroaryl ring selected from the group consisting of oxazolyl, pyridyl, benzthiazolyl and benzoxazolyl, wherein any of the above R₈ can be optionally substituted by one or more R_j;
- 35 R_j is selected from the group consisting of phenyl, methoxycarbonyl, carbamoyl wherein the nitrogen atom may be independently mono or disubstituted by methyl or phenyl; methoxycarbonylamino and halogen, R_j may be further optionally substituted by one or more R_k;
- 40 R_k is selected from the group consisting of phenyl, methoxycarbonyl, carbamoyl, benzyloxycarbonylamino and halogen.

45

11. A compound of formula (Ia):



(Ia)

5

wherein:

A is -C(Y)- or -SO₂-

10

Y is O, S or NR_a wherein R_a is selected from the group consisting of H, alkyl, aryl, alkoxy, aryloxy, alkylamino and arylamino;

15

R₁ is alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl or amino wherein R₁ is optionally substituted by one or more R_b;

20

R_b is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkoxy, aryloxy, alkoxy carbonyl, aryloxycarbonyl, alkanoyl, aroyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkoxy carbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R_b may be further optionally substituted by one or more R_c;

25

30

35

R_c is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocycle, heteroaryl, arylalkyl, alkoxy, aryloxy, arylalkoxy, alkanoyl, aroyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

R₂ is H or alkyl;

40

R₃ is H, alkyl, cycloalkyl, aryl, heterocycl or heteroaryl, wherein R₃ is optionally substituted by one or more groups of the formula R_d;

5 R_d is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocycl, heteroaryl, alkoxy, aryloxy, arylalkoxy, alkoxy carbonyl, aryloxy carbonyl, alkanoyl, aroyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocycl or heteroaryl, alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocycl or heteroaryl, alkoxy carbonylamino, aryloxy carbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocycl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R_d may be further optionally substituted by one or more R_e;

20 R_e is selected from the group consisting of alkyl, cycloalkyl, aryl, arylalkyl, alkoxy, aryloxy, arylalkoxy, alkanoyl, aroyl, amino, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

25 R₄ is H or alkyl;

R₅ is H, alkyl or cycloalkyl;

30 R₆ is H, alkyl, cycloalkyl, aryl, heterocycl or heteroaryl, wherein R₆ is optionally substituted by one or more groups of the formula R_f,

35 R_f is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocycl, heteroaryl, alkoxy, aryloxy, alkanoyl, aroyl, arylalkoxy, heteroarylalkoxy, alkoxy carbonyl, aryloxy carbonyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocycl or heteroaryl, alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylalkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocycl or heteroaryl, alkoxy carbonylamino, aryloxy carbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocycl or heteroaryl, halogen, hydroxy, oxo,

carboxy, cyano, nitro, amidino and guanidino, R_f may be further optionally substituted by one or more R_g;

- 5 R_g is selected from the group consisting of alkyl, cycloalkyl, aryl optionally substituted by halogen, C1-5alkyl or C1-5alkoxy, heterocyclyl, heteroaryl, alkoxy, aryloxy, arylalkoxy, alkoxycarbonyl, aryloxycarbonyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl; alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl; alkoxycarbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, 10 arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl; halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;
- 15 20 or R₅ together with R₆ form a 3 to 6 membered carbocyclic ring, the carbocyclic ring being optionally substituted with one or more R_h;

- 25 R_h is selected from the group consisting of alkyl, aryl, alkoxycarbonyl, aryloxycarbonyl, arylalkoxycarbonyl, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with a group selected from alkyl, cycloalkyl, aryl, arylalkyl, heterocyclyl or heteroaryl; halogen, hydroxy, carboxy and cyano;

- R₇ is R₈-C(Z)-;
- 30 35 wherein Z is O, S, or NR_i; wherein R_i is selected from the group consisting of H, alkyl, aryl, alkoxy, aryloxy and hydroxy;

- R₈ is a 5-8 membered monocyclic heteroaryl or 8-11 membered bicyclic heteroaryl ring system, each of the monocyclic or bicyclic ring systems having 1-4 of the same or different heteroatoms selected from the group consisting of N, O and S wherein any of the above R₈ can be optionally substituted by one or more R_j;

- 40 45 R_j is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, arylalkyl, alkoxy, aryloxy, alkanoyl, aroyl, arylalkoxy, alkoxycarbonyl, aryloxycarbonyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylalkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl;

5 alkoxy carbonylamino, aryloxy carbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocycl or heteroaryl; halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R_j may be further optionally substituted by one or more R_k;

10 R_k is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocycl, heteroaryl, alkoxy, aryloxy, arylalkoxy, alkoxy carbonyl, aryloxy carbonyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocycl or heteroaryl, alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocycl or heteroaryl, alkoxy carbonylamino, aryloxy carbonylamino, 15 arylalkoxy carbonylamino, arylalkoxy carbonylaminoalkyl, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocycl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, wherein R_k may be further optionally substituted by R_j;

20 25 R_j is selected from the group consisting of alkyl, cycloalkyl, aryl, and benzyl;

X is O, S or N-OH;

30 and the pharmaceutically acceptable derivatives thereof;

with the following provisos:

35 when R₆ is alkyl the alkyl must be substituted with R_f wherein R_f is not hydroxy, sulphydryl or halogen;

and

when R₁ is C1alkyl then R_b cannot be carbamoyl, alkanoylamino, aroylamino, ureido, alkoxy carbonylamino, aryloxy carbonylamino, alkylsulfonylamino, arylsulfonylamino, amino, amidino or guanidino wherein each said R_b is linked to said R₁ via the nitrogen atom thereof.

40 45 12. The compound according to claim 11 wherein:

R_a is selected from the group consisting of H, alkyl and aryl;

- R₁ is C1-8 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, pyranyl, thiopyranyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, or amino wherein R₁ is optionally substituted by one or more R_b;
- 5 R_b is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkoxy, aryloxy, C1-8 alkoxy carbonyl, aryloxycarbonyl, C1-8 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkanoylamino, aroylamino, C1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkanoylthio, aroylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, alkoxy carbonylamino, aryloxycarbonylamino, C1-8 alkyl carbamoyloxy, aryl carbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,

thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxyazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R_b may be further optionally substituted by one or more R_c;

R_c is selected from the group consisting of C1-8 alkyl, C3-6 cycloalkyl, 10 aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxyazinyl, 15 C1-8 alkoxy, aryloxy, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

20 R₃ is H, C1-8 alkyl, C3-7 cycloalkyl or aryl wherein R₃ is optionally substituted by one or more R_d;

R_d is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl, 25 heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxyazinyl, 30 C1-8 alkoxy, aryloxy, alkanoyl, aroyl, C1-8 alkoxycarbonyl, aryloxycarbonyl, C1-8 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected 35 from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxyazinyl, 40 C1-8 alkanoylamino, aroylamino, C1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, 45 isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxyazinyl, C1-8 alkanoylthio, aroylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl,

5 piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, alkoxy carbonylamino, aryloxy carbonylamino, C1-8 alkyl carbamoyloxy, aryl carbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R_d may be further optionally substituted by one or more R_e;

10 R_e is selected from the group consisting of C1-8 alkyl, C3-6 cycloalkyl, aryl, arylalkyl, C1-8 alkoxy, aryloxy, arylalkoxy, aroyl, amino, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

15 R₅ is H or alkyl;

20 R₆ is H, C1-8 alkyl, C3-7 cycloalkyl or aryl wherein R₆ is optionally substituted by one or more R_f;

25 R_f is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkoxy, aryloxy, aryl C1-8 alkoxy, heteroaryl C1-8 alkoxy, C1-8 alkoxy carbonyl, aryloxycarbonyl, C1-8 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl,

quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoxyazinyl, C1-8 alkanoylamino, aroylamino, C1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylC1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoxyazinyl, alkoxy carbonylamino, aryloxycarbonylamino, C1-8 alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoxyazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R_f may be further optionally substituted by one or more R_g:

R_g is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl optionally substituted by halogen, C1-3alkyl or C1-3alkoxy; heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoxyazinyl, C1-8 alkoxy, aryloxy, arylC1-8alkoxy, C1-8 alkoxy carbonyl, aryloxycarbonyl, C1-8 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl,

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benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoxyazinyl, C1-8 alkanoylamino, aroylamino, C1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocycl 10 selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl or phenoxyazinyl, 15 alkoxy carbonylamino, aryloxy carbonylamino, C1-8 alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl and arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocycl 20 selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, 25 quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoxyazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

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R_4 is selected from the group consisting of C1-8 alkyl, aryl, C1-8 alkoxy carbonyl, aryloxy carbonyl, arylC1-8alkoxy carbonyl, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with a group selected from C1-8 alkyl, C3-7 cycloalkyl, aryl, arylC1-8alkyl, heterocycl 35 selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoxyazinyl, 40 halogen, hydroxy, oxo, carboxy and cyano;

R_8 is a heteroaryl ring selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, indolizinyl, indolyl, isoindolyl, benzofuranyl,

benzothienyl, indazolyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, tetrazolyl, purinyl, quinolizinyl, quinolinyl, isoquinolinyl, cinnolinyl, phthalazinyl, quinazolinyl, quinoxalinyl, naphthyridinyl, pteridinyl, carbazolyl, acridinyl and phenazinyl, wherein any of the above R₈ can be optionally substituted by one or more R_j;

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R_j is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, arylalkyl, alkoxy, aryloxy, arylalkoxy, alkoxycarbonyl, aryloxycarbonyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independantly mono or di-susbsstituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, arylalkylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, alkoxycarbonylamino, aryloxycarbonylamino, C1-8 alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independantly mono or di-susbsstituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, halogen, hydroxy,

oxo, carboxy, cyano, nitro, amidino and guanidino, R_j may be further optionally substituted by one or more R_k;

R_k is selected from the group consisting of alkyl, cycloalkyl, aryl,
5 heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, 10 benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxyazinyl, alkoxy, aryloxy, arylalkoxy, alkoxycarbonyl, aryloxycarbonyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independantly mono or di-susbsstituted by alkyl, aryl, heterocyclyl selected 15 from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, heteroaryl selected from furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxyazinyl, alkanoylamino, aroylamino, alkylthio 20 wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, heteroaryl selected from furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxyazinyl, 25 alkanoylamino, aroyloxycarbonylamino, arylalkoxycarbonylamino, arylalkoxycarbonylaminooalkyl, C1-8 alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-susbsstituted by alkyl, aryl, heterocyclyl 30 selected from pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, 35 40 45

phenothiazinyl and phenoxazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, wherein R_k may be further optionally substituted by R_i;

5 R₁ is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, phenyl and benzyl;

and

X is O or S.

10

13. The compound according to claim 12 wherein:

15

Y is O or S;

20 R₁ is C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, pyranyl, thiopyranyl, piperazinyl and indolinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl or amino wherein R₁ is optionally substituted by one or more R₅;

25

R_b is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, heteroaryl selected from the group consisting of furanyl, thieryl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny, C1-5 alkoxy, aryloxy, C1-5 alkoxy carbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thieryl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl

or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, 10 piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, 15 amidino and guanidino, R_b may be further optionally substituted by one or more R_c;

20 R_c is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl, aryl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl and pyridinyl, C1-5 alkoxy, aryloxy, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

25 R₂ is H or C1-3 alkyl;

R₃ is H, C1-5 alkyl, C3-7 cycloalkyl or aryl, wherein R₃ is optionally substituted by one or more R_d;

30 R_d is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxy, aryloxy, C1-5 alkanoyle, aroyl, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkanoyle, aroyl, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom

may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxy carbonylamino, aryloxycarbonylamino, C1-5 alkyl carbamoyloxy, aryl carbamoyloxy, C1-5 alkylsulfonylamino, 10 arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected 15 from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R_d may be further optionally substituted by one or more R_e;

20

R_e is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl, aryl, arylalkyl, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, aroyl, amino, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

25

R₄ is H or C1-3 alkyl;

30 R₅ is H or C1-8 alkyl;

R₆ is H, C1-5 alkyl, C3-7 cycloalkyl or aryl wherein R₆ is optionally substituted by one or more R_f;

35

R_f is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, heteroarylC1-5alkoxy, C1-5 alkoxy carbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl,

thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylC1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny, C1-5 alkoxy carbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R_f may be further optionally substituted by one or more R_g;

R_g is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, aryl optionally substituted by halogen, methyl or methoxy; heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, C1-5 alkoxy carbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny, C1-5 alkanoylamino, aroylamino, C1-5

alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, 5 piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, 10 isoquinolinyl, quinazolinyl and quinoxalanyl, C1-5 alkoxy carbonylamino, aryloxycarbonylamino, C1-5 alkyl carbamoyloxy, aryl carbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl 15 selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, 20 isoquinolinyl, quinazolinyl and quinoxalanyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

25 R_h is selected from the group consisting of C1-5 alkyl, aryl, C1-5 alkoxy carbonyl, aryloxycarbonyl, aryl C1-5 alkoxy carbonyl, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with a group selected from C1-5 alkyl, C3-7 cycloalkyl, aryl, aryl C1-5 alkyl, heterocyclyl selected from the group 30 consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and 35 quinoxalanyl, halogen, hydroxy, carboxy and cyano;

R_i is alkoxy, aryloxy or hydroxy;

40 R_g is a heteroaryl ring selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, indolizinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, indazolyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, 45 quinolizinyl, quinolinyl, isoquinolinyl, cinnolinyl, phthalazinyl, quinazolinyl, quinoxalanyl, naphthyridinyl, pteridinyl, carbazolyl, acridinyl and phenazinyl, wherein any of the above R_g can be optionally substituted by one or more R_j ;

R_j is selected from the group consisting of C1-8alkyl, C3-7cycloalkyl, aryl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoazinyl; arylC1-8alkyl, C1-8alkoxy, aryloxy, arylC1-8alkoxy, C1-8alkoxycarbonyl, aryloxycarbonyl, C1-8alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independantly mono or di-susbtituted by C1-8alkyl, aryl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoazinyl, C1-8alkanoylamino, aroylamino, C1-8alkylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, arylC1-8alkylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-8 alkyl, aryl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoazinyl, alkoxy carbonylamino, aryloxycarbonylamino, C1-8 alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-susbtituted by C1-8 alkyl, aryl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R_j may be further optionally substituted by one or more R_k;

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R_k is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, 5 imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkoxy, aryloxy, arylC1-8alkoxy, C1-8alkoxycarbonyl, aryloxycarbonyl, C1-10 8alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independantly mono or di-susbsituted by C1-8alkyl, aryl, heterocyclyl selected from pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, 15 isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, alkanoylamino, aroylamino, C1-20 8alkylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-8alkyl, aryl, heterocyclyl selected from pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, 25 triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8alkoxycarbonylamino, aryloxycarbonylamino, arylC1-30 8alkoxycarbonylamino, arylalkoxycarbonylaminoC1-8alkyl, C1-8alkylcarbamoyloxy, arylcarbamoyloxy, C1-8alkylsulfonylamino, arylsulfonylamino, C1-8alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-susbsituted by C1-8alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, 35 pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8alkoxycarbonylamino, arylalkoxycarbonylaminoC1-8alkyl, C1-8alkylcarbamoyloxy, arylcarbamoyloxy, C1-8alkylsulfonylamino, arylsulfonylamino, C1-8alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-susbsituted by C1-8alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, 40 pyrrolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, where R_k may be further optionally substituted by R₁. 45

5 14. The compound according to claim 13 wherein:

Y is O;

10 R_1 is C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocycl selected from the group consisting of piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, pyranyl and thiopyranyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, or amino wherein R_1 is optionally substituted by one or more R_b ;

15 R_b is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl; C1-5 alkoxy, aryloxy, C1-5 alkoxy carbonyl, aryloxy carbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl, naphthyl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl or aryl; C1-5 alkoxy carbonylamino, aryloxy carbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy, cyano and nitro, R_b may be further optionally substituted by one or more R_c ;

45 R_c is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl, aryl, C1-5 alkoxy, aryloxy, halogen, hydroxy, oxo, carboxy, and cyano;

R₂ is H or methyl;

R₃ is H, C1-5 alkyl, C3-7 cycloalkyl or phenyl, wherein R₃ is optionally substituted by one or more R_d;

5

R_d is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5 alkoxy, aryloxy, aroyl, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy and cyano, R_d may be further optionally substituted by one or more R_e;

R_e is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl, aryl, arylC1-5alkyl, C1-5 alkoxy, aryloxy, arylC1-3alkoxy, aroyl, amino, halogen, hydroxy, oxo, carboxy and cyano;

40

R₄ is H or methyl;

45

R₅ is H or C1-5 alkyl;

R₆ is H, C1-5 alkyl, C3-7 cycloalkyl, phenyl or naphthyl wherein R₆ is optionally substituted by one or more R_f;

5

R_f is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, pyridylC1-5alkoxy, thienylC1-5alkoxy, furanylC1-5alkoxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylC1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy and cyano, R_f may be further optionally substituted by one or more R_g;

40

R_g is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, phenyl optionally substituted by halogen, methyl or methoxy; naphthyl optionally substituted by halogen, methyl or methoxy; heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl,

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pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl,
benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and
quinoxalinyl, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, C1-5
alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl
5 wherein the nitrogen atom may be independently mono or di-substituted
by C1-5 alkyl, aryl, heterocycl selected from the group consisting of
piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the
group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl,
imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl,
10 benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl,
C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom
may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom
may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen
atom may be independently substituted by C1-5 alkyl, aryl, heterocycl
15 selected from the group consisting of piperidinyl, morpholinyl and
piperazinyl or heteroaryl selected from the group consisting of furanyl,
thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl,
benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl,
quinolinyl, isoquinolinyl, C1-5 alkoxy carbonylamino,
20 aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5
alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl,
arylaminosulfonyl, amino wherein the nitrogen atom may be
independently mono or di-substituted by C1-5 alkyl, aryl, heterocycl
25 selected from the group consisting of pyrrolidinyl, piperidinyl,
morpholinyl and piperazinyl or heteroaryl selected from the group
consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl,
pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl,
benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, halogen,
hydroxy, oxo, carboxy and cyano;
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R_h is selected from the group consisting of C1-5 alkyl, phenyl, naphthyl, C1-5
alkoxycarbonyl, aryloxycarbonyl, arylC1-3alkoxycarbonyl, carbamoyl wherein
35 the nitrogen atom may be optionally mono or di-substituted with a group selected
from C1-5 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, arylC1-3alkyl, heterocycl
selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and
piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl,
pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl,
40 benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and
isoquinolinyl, halogen, hydroxy, carboxy and cyano;

45 Z is O or S;

- R₈ is a heteroaryl ring selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, indolizinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, indazolyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolizinyl, quinolinyl, isoquinolinyl, cinnolinyl, phthalazinyl, quinazolinyl, quinoxalinyl, naphthyridinyl, pteridinyl, carbazolyl, acridinyl and phenazinyl, wherein any of the above R₈ can be optionally substituted by one or more groups of the formula R_j;
- 10 R_j is selected from the group consisting of C1-5alkyl, C3-6cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, arylC1-5alkyl, C1-5alkoxy, aryloxy, arylC1-5alkoxy, C1-5alkoxycarbonyl, aryloxycarbonyl, C1-5alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5alkyl, aryl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl, heteroaryl selected from furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5alkanoylamino, aroylamino, C1-5alkylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, arylC1-5alkylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5alkylsulfonylamino, arylsulfonylamino, C1-5alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, wherein R_j may be further optionally substituted by one or more R_k;
- 45 R_k is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, tetrazolyl,

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pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, C1-3 alkoxy, aryloxy, arylC1-3alkoxy, C1-3alkoxycarbonyl, aryloxycarbonyl, C1-3alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independantly mono or di-susbsstituted by C1-3 alkyl, aryl, heterocycl selected from the group consisting of morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, and pyridinyl, C1-3alkanoylamino, aroylamino, C1-3alkylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-3alkyl, phenyl, naphthyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl and pyridinyl, C1-3alkoxycarbonylamino, aryloxycarbonylamino, arylC1-3alkoxycarbonylamino, benzylloxycarbonylaminoC1-5alkyl, C1-3 alkylcarbamoyloxy, arylcarbamoyloxy, C1-3alkylsulfonylamino, arylsulfonylamino, C1-3alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-susbsstituted by C1-3alkyl, aryl, heterocycl selected from the group consisting of pyrrolidinyl, 10

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piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy, cyano and nitro, wherein R_k may be further optionally substituted by R_l;

25

R_l is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl and phenyl.

30

15. The compound according to claim 14 wherein:

35

R_l is C1-5 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocycl selected from the group consisting of piperidinyl, morpholinyl, piperazinyl, pyranyl and thiopyranyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, or amino, wherein R_l is optionally substituted by one or more R_b;

45

R_b is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl, heteroaryl selected from the group

consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-3 alkoxy, phenoxy, C1-3
 5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-3 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom
 10 may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5alkyl, phenyl or naphthyl; C1-5 alkoxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy and cyano, R_b may be further optionally substituted by one or more R_c;

25 R_c is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, aryl, C1-3 alkoxy, phenoxy, halogen, hydroxy, oxo, carboxy and cyano;

R₂ is H;

30 R₃ is C1-5 alkyl, C3-6 cycloalkyl or phenyl, wherein R₃ is optionally substituted by one or more R_d;

35 R_d is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, quinolinyl andisoquinolinyl, C1-5 alkoxy, phenoxy, aroyl, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, C1-5 alkanoylamino, aroylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, phenylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-3 alkyl, phenyl or heteroaryl selected the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl
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- and indolyl, C1-5 alkoxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, phenyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, halogen, hydroxy, oxo, carboxy and cyano, R_d may be further optionally substituted by one or more R_e;
- 5
- 10 R_e is selected from the group consisting of C1-5 alkyl, C5-6 cycloalkyl, phenyl, naphthyl, arylC1-3alkyl, C1-5 alkoxy, phenoxy, arylC1-3alkoxy, aroyl, amino, halogen, hydroxy, oxo, carboxy and cyano;
- 15 wherein the configuration at the stereocenter defined by R₂ and R₃ and the carbon they are attached to is L;
- R₄ is H;
- 20 R₅ is H or C1-3 alkyl;
- 25 R₆ is H, C1-5 alkyl, C3-6 cycloalkyl or phenyl. wherein R₆ is optionally substituted by one or more R_f;
- R_f is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, 30 piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-5 alkoxy, aryloxy, arylC1-3alkoxy, pyridylC1-5alkoxy, thienylC1-5alkoxy, furanylC1-5alkoxy, C1-5 alkoxycarbonyl, 35 aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, C1-5 alkanoylamino, aroylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a 40 sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylC1-3alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl or phenyl; C1-5 alkoxycarbonylamino, C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl, naphthyl, 45 heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and

piperazinyl or heteroaryl selected from the group consisting of furanyl, thieryl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, halogen, hydroxy, oxo, carboxy and cyano, R_f may be further optionally substituted by one or more R_g;

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R_g is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl optionally substituted by halogen, methyl or methoxy; heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thieryl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, pyrimidinyl, pyrazinyl and indolyl, C1-5 alkoxy, aryloxy, arylC1-3alkoxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or aryl; C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl or aryl; C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or aryl; halogen, hydroxy, oxo, carboxy and cyano;

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R_h is selected from the group consisting of C1-5 alkyl, phenyl, C1-5 alkoxycarbonyl, aryloxycarbonyl, arylC1-3alkoxycarbonyl, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with C1-5 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, arylC1-3alkyl, halogen, hydroxy, carboxy and cyano;

wherein Z is O;

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R_g is a heteroaryl ring selected from the group consisting of oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, wherein any of the above R_g can be optionally substituted by one or more R_j;

R_j is selected from the group consisting of C1-5 alkyl, C5-6 cycloalkyl, phenyl, naphthyl, pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, furanyl, thieryl, pyrrolyl, tetrazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, arylC1-

3alkyl, C1-3alkoxy, aryloxy, arylC1-3alkoxy, C1-3alkoxycarbonyl, aryloxycarbonyl, C1-3alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independantly mono or di-susbtituted by C1-3alkyl, phenyl, naphthyl, piperidinyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl; C1-3alkanoylamino, aroylamino, C1-3alkylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, arylC1-3alkylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-3 alkyl, phenyl, naphthyl, piperidinyl, morpholiny, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl; C1-3alkoxycarbonylamino, aryloxycarbonylamino, C1-3 alkylcarbamoyloxy, arylcarbamoyloxy, C1-3alkylsulfonylamino, arylsulfonylamino, C1-3alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-susbtituted by C1-3 alkyl, phenyl, naphthyl, piperidinyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl; halogen, hydroxy, oxo, carboxy, cyano and nitro, R_j may be further optionally substituted by one or more R_k;

R_k is selected from the group consisting of methyl, C5-6 cycloalkyl, phenyl, pyrrolidinyl, piperidinyl, morpholiny, piperazinyl, furanyl, thienyl, pyrrolyl, tetrazolyl, pyridinyl, pyrimidinyl, C1-3 alkoxy, phenoxy, benzyloxy, methoxycarbonyl, acetyloxy, benzoxyloxy, carbamoyl wherein the nitrogen atom may be independantly mono or di-susbtituted by C1-3 alkyl, phenyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl or pyridinyl; acetylarnino, benzoylamino, methylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by methyl, phenyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl or pyridinyl; arylC1-3alkoxycarbonylamino, benzyloxycarbonylaminoC1-5alkyl, methylcarbamoyloxy, amino wherein the nitrogen atom may be independently mono or di-susbtituted by C1-3alkyl, phenyl, naphthyl, pyrrolidinyl, piperidinyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, pyrimidinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl or isoquinolinyl, halogen, hydroxy, oxo, carboxy, cyano and nitro, wherein R_k may be further optionally substituted by R_l;

R_l is selected from the group consisting of C1-3 alkyl,C3-6 cycloalkyl and phenyl.

16. The compound according to claim 15 wherein:

5 R₁ is C1-3 alkyl, C5-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl, piperazinyl, pyranyl and thiopyranyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, or amino, wherein R₁ is optionally substituted by one or more R_b;

10 R_b is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl, C1-3 alkoxy, C1-3 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, phenyl or heteroaryl selected from the group consisting of pyrrolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl and benzthiazolyl; C1-5 alkanoylamino, aroylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-3 alkyl or phenyl; C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, phenyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of pyrrolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, quinolinyl and isoquinolinyl; halogen, hydroxy, oxo, carboxy and cyano, R_b may be further optionally substituted by one or more R_c;

R_c is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, C1-3 alkoxy, halogen and hydroxy;

35 R₃ is C1-5 alkyl, C5-6 cycloalkyl or phenyl wherein R₃ is optionally substituted by one or more R_d;

40 R_d is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, 4-piperidinyl, 4-morpholinyl, piperazinyl, furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-5 alkoxy, phenoxy, aroyl, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or phenyl; C1-5 alkanoylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-3 alkyl or phenyl; C1-5 alkylsulfonylamino, C1-5 alkoxycarbonylamino, C1-5

alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; halogen, hydroxy, oxo, carboxy and cyano, R_d may be further optionally substituted by one or more R_c;

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R_e is selected from the group consisting of C1-5 alkyl, C5-6 cycloalkyl, phenyl, benzyl, C1-5 alkoxy, phenoxy, benzyloxy, aroyl, halogen, hydroxy, oxo, carboxy and cyano;

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R₆ is H, C1-5 alkyl or phenyl wherein R₆ is optionally substituted by one or more R_f,

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R_f is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-3 alkoxy, benzyloxy, pyridyl, C1-3alkoxy, thienylC1-3alkoxy, furanylC1-3alkoxy, C1-3 alkoxycarbonyl, phenoxyoxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; C1-5 alkanoylamino, aroylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl or phenyl; C1-3 alkoxycarbonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or phenyl; halogen, hydroxy, oxo, carboxy and cyano, R_f may be further optionally substituted by one or more R_g;

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R_g is selected from the group consisting of C1-3 alkyl, phenyl optionally substituted by halogen, methyl or methoxy; heterocycl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl and pyridinyl, C1-3 alkoxy, aryloxy, benzyloxy, C1-5 alkoxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or phenyl; C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl or phenyl; C1-5 alkoxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-3 alkylsulfonylamino, arylsulfonylamino, C1-3 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; halogen, hydroxy, oxo, carboxy and cyano;

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R_h is selected from the group consisting of C1-3 alkyl, phenyl, C1-3 alkoxycarbonyl, phenoxyoxycarbonyl, benzyloxy, carbamoyl wherein the

nitrogen atom may be optionally mono or di-substituted with C1-5 alkyl, phenyl, benzyl, halogen, hydroxy, carboxy and cyano;

- 5 R₈ is a heteroaryl ring selected from the group consisting of oxazolyl, thiazolyl, imidazolyl, pyrazolyl, pyridyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoazazolyl, quinolinyl and isoquinolinyl, wherein any of the above R₈ can be optionally substituted by one or more R_j;
- 10 R_j is selected from the group consisting of C1-5 alkyl, C5-6 cycloalkyl, phenyl, naphthyl, pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, furanyl, thienyl, pyrrolyl, tetrazolyl, pyridinyl, pyrimidinyl, benzyl, C1-3alkoxy, phenoxy, benzyloxy, C1-3alkoxycarbonyl, acetyloxy, benzoyloxy, carbamoyl wherein the nitrogen atom may be independantly mono or di-susbsituted by methyl, phenyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl and pyridinyl; acetylarnino, benzoylarnino, methylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by methyl, phenyl, thiazolyl, imidazolyl and pyridinyl; C1-3 alkoxycarbonylarnino, C1-3 alkylcarbamoyloxy, arylcarbamoyloxy, C1-3alkylsulfonylarnino, arylsulfonylarnino, amino wherein the nitrogen atom may be independently mono or di-susbsituted by methyl, phenyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl and pyridinyl; halogen, hydroxy, carboxy, cyano and nitro, R_j may be further optionally substituted by one or more R_k;
- 15 R_k is selected from the group consisting of methyl, C5-6 cycloalkyl, phenyl, pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, furanyl, thienyl, pyrrolyl, pyridinyl, C1-3 alkoxy, phenoxy, benzyloxy, methoxycarbonyl, acetyloxy, benzoyloxy, carbamoyl wherein the nitrogen atom may be independantly mono or di-susbsituted by methyl, phenyl, furanyl, thienyl; acetylarnino, benzoylarnino, methylthio wherein the sulfur atom may be oxidised to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by methyl, phenyl, furanyl, thienyl, pyrrolyl, oxazolyl and thiazolyl, benzoyloxycarbonylarnino, benzoyloxycarbonylarninoC1-5alkyl, amino wherein the nitrogen atom may be independently mono or di-susbsituted by C1-3alkyl, phenyl, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl and pyridinyl, halogen, hydroxy, carboxy, cyano and nitro, wherein R_k may be further optionally substituted by R_i;
- 20 R_i is selected from the group consisting of C1-3 alkyl,C3-6 cycloalkyl and phenyl.
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17. The compound according to claim 16 wherein:

5 R₁ is C5-6 cycloalkyl, phenyl, naphthyl, piperidinyl, morpholinyl, piperazinyl, furanyl, thienyl, pyrrolyl, pyranyl, thiopyranyl or amino wherein R₁ is optionally substituted by one or more R_b;

10 R_b is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl, furanyl, thienyl, pyrrolyl, imidazolyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, C1-3 alkoxy, C1-3 alkoxycarbonyl, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; C1-5 alkanoylamino, aroylamino, ureido wherein either nitrogen atom may be independently substituted by C1-3alkyl or phenyl; C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3alkyl or phenyl;, 15 halogen, hydroxy, oxo, carboxy and cyano, R_b may be further optionally substituted by one or more R_c;

20 R_c is selected from the group consisting of C1-3 alkyl, C1-3 alkoxy, halogen and hydroxy;

25 R_d is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, 4-piperidinyl, furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-3alkoxy, C1-5alkoxycarbonyl, C1-5alkanoyloxy, benzoxyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3alkyl or phenyl; C1-5alkanoylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, C1-3alkoxycarbonylamino, C1-3alkylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, halogen, hydroxy, oxo, carboxy and cyano, R_d may be further optionally substituted by one or more R_e;

30 35 R_e is selected from the group consisting of C1-3 alkyl, phenyl, benzyl, C1-3 alkoxy, phenoxy, benzyloxy, benzoyl, halogen, hydroxy, oxo, carboxy and cyano;

R_f is H or methyl;

40 R₆ is C1-5 alkyl or phenyl, wherein R₆ is optionally substituted by one or more groups of the formula R_f,

45 R_f is selected from the group consisting of methyl, C3-6 cycloalkyl, phenyl, naphthyl, furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-3 alkoxy, benzyloxy, C1-5 alkanoylamino, aroylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom

may be oxidized to a sulfoxide or sulfone, C1-3 alkoxy carbonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or phenyl; halogen, hydroxy, oxo, carboxy and cyano, R_f may be further optionally substituted by one or more R_g;

5

R_g is selected from the group consisting of C1-3 alkyl, phenyl optionally substituted by halogen or methyl; C1-3 alkoxy, aryloxy, benzyloxy, C1-3 alkoxy carbonyl, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; C1-5 alkanoylamino, arylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; halogen, hydroxy, oxo, carboxy and cyano;

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R_h is selected from the group consisting of C1-3 alkyl, phenyl, C1-3 alkoxy carbonyl, benzyloxy and carboxy;

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R_g is a heteroaryl ring selected from the group consisting of oxazolyl, thiazolyl, imidazolyl, pyrazolyl, pyridyl, benzimidazolyl, benzthiazolyl and benzoxazolyl, wherein any of the above R_g can be optionally substituted by one or more R_j;

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R_j is selected from the group consisting of C1-5 alkyl, cyclohexyl, phenyl, piperidinyl, furanyl, thienyl, pyridinyl, benzyl, methoxy, phenoxy, benzyloxy, methoxycarbonyl, acetoxy, benzoyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by methyl, phenyl, furanyl, thienyl; acetyl amino, benzoyl amino, ureido wherein either nitrogen atom may be independently substituted by methyl or phenyl; methoxycarbonylamino, C1-3 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by methyl, phenyl, furanyl or thienyl; halogen, hydroxy, carboxy and cyano, R_j may be further optionally substituted by one or more R_k;

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R_k is selected from the group consisting of methyl, C5-6 cycloalkyl, phenyl, piperidinyl, piperazinyl, furanyl, thienyl, C1-3 alkoxy, phenoxy, benzyloxy, methoxycarbonyl, acetoxy, benzoyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by methyl or phenyl; acetyl amino, benzoyl amino, ureido wherein either nitrogen atom may be independently substituted by methyl or phenyl; benzyloxycarbonylamino, benzyloxycarbonylamino C1-5 alkyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, phenyl, furanyl, or thienyl; halogen, hydroxy, carboxy, cyano and nitro, wherein R_k may be further optionally substituted by R_l;

45

R_l is selected from the group consisting of methyl, C3-6 cycloalkyl and phenyl.

5 18. The compound according to claim 7 wherein:

A is -C(O)- or -SO₂-;

10 R₁ is cyclohexyl, phenyl, naphthyl, piperidinyl, morpholinyl, piperazinyl, pyranyl, thiopyranyl or amino, wherein R₁ is optionally substituted by one or more R_b;

15 R_b is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl, furanyl, thienyl, pyrrolyl, imidazolyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, C1-3 alkoxy, C1-3 alkoxycarbonyl, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; C1-5 alkanoylamino, aroylamino, C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl; halogen, hydroxy, oxo, carboxy and cyano, R_b may be further optionally substituted by one or more R_c;

20 R_c is selected from the group consisting of C1-3 alkoxy, halogen and hydroxy;

25 R₃ is C1-5 alkyl or C5-6 cycloalkyl, wherein R₃ is optionally substituted by one or more R_d;

30 R_d is selected from the group consisting of methyl, C3-6 cycloalkyl, phenyl, thienyl, imidazolyl, pyridinyl, indolyl, C1-4 alkoxy, C1-5 alkanoylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, halogen, hydroxy, oxo, carboxy and cyano, R_d may be further optionally substituted by one or more R_e;

35 R_e is selected from the group consisting of methyl, phenyl, benzyl, methoxy, phenoxy, benzyloxy, benzoyl, halogen and hydroxy;

40 R_f is selected from the group consisting of C3-6 cycloalkyl, phenyl, naphthyl, thienyl, imidazolyl, pyridinyl, indolyl, methoxy, benzyloxy, C1-3 alkanoylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, methoxycarbonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl; halogen, hydroxy, carboxy and cyano, R_f may be further optionally substituted by one or more R_g;

45 R_g is selected from the group consisting of methyl, phenyl optionally substituted by halogen or methyl; methoxy, phenoxy, benzyloxy, methoxycarbonyl, amino wherein the nitrogen atom may be independently

mono or di-substituted by C1-3 alkyl or phenyl; halogen, hydroxy and carboxy;

5 R₈ is a heteroaryl ring selected from the group consisting of oxazolyl, thiazolyl, imidazolyl, pyridyl, benzthiazolyl and benzoxazolyl, wherein any of the above R₈ can be optionally substituted by one or more R_j;

10 R_j is selected from the group consisting of C1-5 alkyl, phenyl, furanyl, thieryl, piperidinyl, pyridinyl, benzyl, methoxy, methoxycarbonyl, acetoxy, benzyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-
15 substituted by methyl or phenyl; acetyl amino, benzoyl amino, ureido wherein either nitrogen atom may be independently substituted by methyl or phenyl; methoxycarbonyl amino, amino wherein the nitrogen atom may be independently mono or di-substituted by methyl, phenyl; halogen, hydroxy, carboxy and cyano, R_j may be further optionally substituted by one or more R_k; and

20 R_k is selected from the group consisting of methyl, C5-6 cycloalkyl, phenyl, piperidinyl, methoxy, phenoxy, benzyloxy, methoxycarbonyl, carbamoyl wherein the nitrogen atom may be independently mono or di-
25 substituted by methyl or phenyl; ureido wherein either nitrogen atom may be independently substituted by methyl or phenyl; benzyloxycarbonyl amino, benzyloxycarbonyl amino C1-5alkyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3alkyl, phenyl, furanyl and thieryl; halogen, hydroxy, carboxy, cyano and nitro, wherein R_k may be further optionally substituted by R_l;

30 R_l is selected from the group consisting of methyl and phenyl.

30

19. The compound according to claim 18 wherein:

35 R₁ is cyclohexyl, phenyl, naphthyl, piperidinyl, morpholinyl, piperazinyl, pyranyl or thiopyranyl, wherein R₁ is optionally substituted by one or more R_b;

40 R_b is selected from the group consisting of, pyrrolyl, imidazolyl, indolyl, benzimidazolyl, methoxy, methoxycarbonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl; halogen, hydroxy and carboxy, R_b may be further optionally substituted by one or more R_c;

45 R_c is selected from the group consisting of methoxy, halogen and hydroxy;

45

R_d is selected from the group consisting of methyl, C3-6 cycloalkyl, phenyl, C1-4 alkoxy, C1-3 alkanoyl amino, methylthio wherein the sulfur atom may be oxidized

to a sulfoxide or sulfone, halogen, hydroxy, oxo, carboxy and cyano, R_d may be further optionally substituted by one or more R_e;

5 R_e is selected from the group consisting of methyl, phenyl, methoxy, halogen and hydroxy;

R_f is H;

10 R_f is selected from the group consisting of C5-6 cycloalkyl, phenyl, naphthyl, thienyl, indolyl, methoxy, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, methoxycarbonylamino, halogen, hydroxy, carboxy and cyano, R_f may be further optionally substituted by one or more R_g;

15 R_g is selected from the group consisting of methyl, phenyl optionally substituted by halogen; methoxy, phenoxy, benzyloxy, methoxycarbonyl, halogen, hydroxy and carboxy;

20 R_g is a heteroaryl ring selected from the group consisting of oxazolyl, thiazolyl, pyridyl, benzthiazolyl and benzoxazolyl, wherein any of the above R_g can be optionally substituted by one or more R_j;

25 R_j is selected from the group consisting of C1-5 alkyl, phenyl, piperidinyl, pyridinyl, benzyl, methoxy, methoxycarbonyl, acetoxy, benzyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by methyl or phenyl; methoxycarbonylamino, halogen, hydroxy and carboxy, R_j may be further optionally substituted by one or more R_k;

30 R_k is selected from the group consisting of methyl, C5-6 cycloalkyl, phenyl, piperidinyl, methoxy, methoxycarbonyl, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by methyl or phenyl; benzyloxycarbonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by methyl or phenyl; halogen, hydroxy and carboxy.

35

20. The compound according to claim 9 wherein:

40

R₁ is phenyl or 4-morpholinyl, wherein R₁ is optionally substituted by one or more R_b;

45

R_b is selected from the group consisting of benzimidazolyl, methoxy and dimethylamino, R_b may be further optionally substituted by a halogen atom;

R₃ is C1-5 alkyl wherein R₃ is optionally substituted by one or more R_d;

R_d is selected from the group consisting of C3-6 cycloalkyl and phenyl, R_d may be further optionally substituted by one or more R_e;

5 R_e is selected from the group consisting of methyl and halogen;

R₆ is C1-5 alkyl optionally substituted by one or more R_f;

10 R_f is selected from the group consisting of C5-6 cycloalkyl, phenyl, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, and halogen, R_f may be further optionally substituted by one or more R_g;

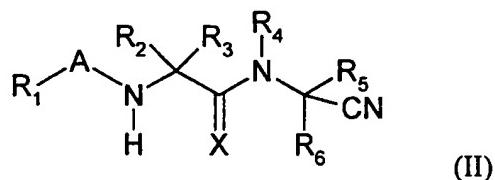
R_g is selected from the group consisting of methyl, methoxy, methoxycarbonyl, halogen and hydroxy;

15 R₈ is a heteroaryl ring selected from the group consisting of oxazolyl, pyridyl, benzthiazolyl and benzoxazolyl, wherein any of the above R₈ can be optionally substituted by one or more R_j;

20 R_j is selected from the group consisting of C1-5 alkyl, phenyl, pyridinyl, piperidinyl, methoxycarbonyl, carbamoyl wherein the nitrogen atom may be independantly mono or disubstituted by methyl or phenyl; methoxycarbonylamino and halogen, R_j may be further optionally substituted by one or more R_k;

25 R_k is selected from the group consisting of methyl, C5-6 cycloalkyl, phenyl, methoxycarbonyl, carbamoyl, benzyloxycarbonylamino and halogen.

30 21. A compound of the formula (II):



wherein:

40 A is -C(Y)- or -SO₂-

Y is O, S or NR_a wherein R_a is selected from the group consisting of H, alkyl, aryl, alkoxy, aryloxy, alkylamino and arylamino;

- 5 R₁ is alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl or amino wherein R₁ is optionally substituted by one or more R_b;

R_b is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkoxy, aryloxy, alkanoyl, aroyl, alkoxycarbonyl, aryloxycarbonyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkoxycarbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino; R_b may be further optionally substituted by one or more R_c;

25 R_c is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, arylalkyl, alkoxy, aryloxy, arylalkoxy, alkanoyl, aroyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

30 R₂ is H or alkyl;

35 R₃ is H, alkyl, cycloalkyl, aryl, heterocyclyl or heteroaryl, wherein R₃ is optionally substituted by one or more R_d;

R_d is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkoxy, aryloxy, arylalkoxy, alkoxycarbonyl, aryloxycarbonyl, alkanoyl, aroyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkoxycarbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano,

nitro, amidino and guanidino, R_d may be further optionally substituted by one or more R_e;

5 R_e is selected from the group consisting of alkyl, cycloalkyl, aryl, arylalkyl, alkoxy, aryloxy, arylalkoxy, alkanoyl, aroyl, amino, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

R₄ is H or alkyl;

10

R₅ is H or alkyl;

15 R₆ is H, alkyl, cycloalkyl, aryl, heterocyclyl, aryl, heteroaryl or cyano, wherein R₆ is optionally substituted by one or more R_f,

20 R_f is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkoxy, aryloxy, arylalkoxy, alkanoyl, aroyl, alkoxycarbonyl, aryloxycarbonyl, alkanoyloxy, aroyloxy, heteroarylalkoxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkanoylamino, aroylamino, alkylcarbamoyl, arylcarbamoyl, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylalkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkoxycarbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R_f may be further optionally substituted by one or more R_g;

35 R_g is selected from the group consisting of alkyl, cycloalkyl, aryl optionally substituted by one or more groups selected from halogen, methyl or methoxy, heterocyclyl, heteroaryl, alkoxy, aryloxy, arylalkoxy, alkoxycarbonyl, aryloxycarbonyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkanoylamino, aroylamino, alkylcarbamoyl, arylcarbamoyl, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkoxycarbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino,

40

45

arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

5

or R₅ together with R₆ form a 3 to 6 membered carbocyclic ring, the carbocyclic ring being optionally substituted with one or more R_h;

10 R_h is selected from the group consisting of alkyl, aryl, alkoxycarbonyl, aryloxycarbonyl, arylalkoxycarbonyl, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with a group selected from alkyl, cycloalkyl, aryl, arylalkyl, heterocyclyl, heteroaryl, halogen, hydroxy, carboxy and cyano;

15

X is O, S or N-OH; and
the pharmaceutically acceptable derivatives thereof;

20 with the proviso that when Y is O and R₆ is arylalkyl or heteroarylalkyl then R₁ cannot be alkyl, cycloalkyl, aryl, heteroaryl, cycloalkyl-alkyl, aryl-alkyl or aryl-cycloalkyl.

25

22. The compound according to claim 21 wherein:

30

Y is O, S or NR_a wherein R_a is H, alkyl or aryl;

35

R₁ is C1-8alkyl, C3-7cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, indolinyl, pyranyl and thiopyranyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl, phenoxyazinyl, and amino wherein R₁ is optionally substituted by one or more R_b;

40

45

R_b is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl, phenoxyazinyl, and amino wherein R₁ is optionally substituted by one or more R_b,

benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl or phenoxyazinyl, C1-8 alkoxy, aryloxy, C1-8 alkoxy carbonyl, aryloxycarbonyl, C1-8 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxyazinyl, C1-8 alkanoylamino, aroylamino, C1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl or phenoxyazinyl, alkoxy carbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, pyrazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxyazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino, guanidino; R_b may be further optionally substituted by one or more R_c;

R_c is selected from the group consisting of C1-8 alkyl, C3-6 cycloalkyl, aryl, C1-8 alkoxy, aryloxy, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

40

R₃ is H, C1-8 alkyl, C3-7 cycloalkyl, aryl wherein R₃ is optionally substituted by one or more R_d;

45

R_d is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, 5 pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxyazinyl, C1-8 alkoxy, aryloxy, alkanoyl, aroyl, C1-8 alkoxycarbonyl, aryloxycarbonyl, C1-8 10 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group 15 consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxyazinyl, C1-8 20 alkanoylamino, aroylamino, C1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group 25 consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxyazinyl, alkoxycarbonylamino, 30 aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl 35 selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxyazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino, 40 guanidino, R_d may be further optionally substituted by one or more R_e;

R_e is selected from the group consisting of C1-8 alkyl, C3-6 cycloalkyl, aryl, arylalkyl, C1-8 alkoxy, aryloxy, arylalkoxy, aroyl, amino, halogen, 45 hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

R₆ is H, C1-8 alkyl, C3-7 cycloalkyl, aryl or cyano, wherein R₆ is optionally substituted by one or more R_f;

- 5 R_f is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkoxy, aryloxy, arylC1-8alkoxy, heteroarylC1-8alkoxy, C1-8 alkoxycarbonyl, aryloxycarbonyl, C1-8 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkanoylamino, aroylamino, C1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylC1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, alkoxycarbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R_f may be further optionally substituted by one or more R_g;

R_g is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl,
5 aryl optionally substituted by one or more groups selected from halogen,
methyl or methoxy, heterocyclyl selected from the group consisting of
pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and
indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl,
10 pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl,
isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl,
pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl,
benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl,
isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and
phenoxazinyl, C1-8 alkoxy, aryloxy, arylC1-8alkoxy, C1-8
15 alkoxycarbonyl, aryloxycarbonyl, C1-8 alkanoyloxy, aroyloxy, carbamoyl
wherein the nitrogen atom may be independently mono or di-substituted
by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of
pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and
indolinyl, or heteroaryl selected from the group consisting of furanyl,
20 thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl,
isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl,
pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl,
benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl,
isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and
phenoxazinyl, C1-8 alkanoylamino, aroylamino, C1-8 alkylthio wherein
25 the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein
the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein
either nitrogen atom may be independently substituted by alkyl, aryl,
heterocyclyl selected from the group consisting of pyrrolidinyl,
piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or
30 heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl,
oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl,
oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl,
pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl,
benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl,
35 quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoxazinyl,
alkoxycarbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy,
arylcaramoyloxy, alkylsulfonylamino, arylsulfonylamino,
alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom
may be independently mono or di-substituted by alkyl, aryl, heterocyclyl
40 selected from the group consisting of pyrrolidinyl, piperidinyl,
morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl
selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,
thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl,
triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl,
45 pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl,
benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl,

quinoxalinyl, carbazolyl, phenothiazinyl and phenoazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino, and guanidino;

5 R_h is selected from the group consisting of C1-8 alkyl, aryl, C1-8 alkoxycarbonyl, aryloxycarbonyl, arylC1-8alkoxycarbonyl, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with a group selected from C1-8 alkyl, C3-7 cycloalkyl, aryl, arylC1-8alkyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thieryl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, 10 oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoazinyl, halogen, hydroxy, carboxy, and cyano; and

15 X is O or S.

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23. The compound according to claim 22 wherein:

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Y is O or S;

30 R₁ is C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, indolinyl, pyranlyl and thiopyranlyl, heteroaryl selected from the group consisting of furanyl, thieryl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl or amino; 35 wherein R1 is optionally substituted by one or more R_b;

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R_b is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl;, heteroaryl selected from the group consisting of furanyl, thieryl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxy, aryloxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8 45 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl

selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny, C1-5 alkoxy carbonylamino, aryloxy carbonylamino, C1-5 alkyl carbamoyloxy, aryl carbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R_b may be further optionally substituted by one or more R_c;

R_c is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl, aryl, C1-5 alkoxy, aryloxy, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

R₂ is H or C1-3 alkyl;

R₃ is H, C1-5 alkyl, C3-7 cycloalkyl, aryl wherein R₃ is optionally substituted by one or more R_d;

R_d is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny, C1-5 alkoxy carbonyl, aryloxy carbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,

thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, 5 arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected 10 the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny, C1-5 alkoxy carbonylamino, aryloxy carbonylamino, C1-5 alkyl carbamoyloxy, aryl carbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, 15 arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny, halogen, 20 hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R_d may be further optionally substituted by one or more R_e;

25 R_e is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl, aryl, arylalkyl, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, aroyl, amino, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

30 R₄ is H or C1-3 alkyl

35 R₅ is H or C1-8 alkyl

R₆ is H, C1-5 alkyl, C3-7 cycloalkyl, aryl or cyano, wherein R₆ is optionally substituted by one or more R_f;

40 R_f is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, 45 quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny, C1-5 alkoxy, aryloxy, arylC1-5alkoxy,

heteroarylC1-5alkoxy, C1-5 alkoxy carbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, 5 pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be 10 oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylC1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from the 15 group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny, C1-5 alkoxy carbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, 20 arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected 25 from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R_f may be further optionally substituted by 30 one or more R_g;

R_g is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, aryl optionally substituted by one or more groups selected from halogen, 35 methyl or methoxy, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, C1-5 alkoxy carbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl where 40in the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, 45

pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl,
benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and
quinoxalinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein
the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein
the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein
either nitrogen atom may be independently substituted by C1-5 alkyl, aryl,
heterocycl selected from the group consisting of pyrrolidinyl,
piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolyl, or
heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl,
oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl,
pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl,
benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl,
C1-5 alkoxy carbonylamino, aryloxycarbonylamino, C1-5
alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino,
arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino
wherein the nitrogen atom may be independently mono or di-substituted
by C1-5 alkyl, aryl, heterocycl selected from the group consisting of
pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and
indolyl, or heteroaryl selected from the group consisting of furanyl,
thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl,
pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl,
benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and
quinoxalinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and
guanidino;

25

R_h is selected from the group consisting of C1-5 alkyl, aryl, C1-5 alkoxy carbonyl,
aryloxycarbonyl, arylC1-5alkoxy carbonyl, carbamoyl wherein the nitrogen atom
may be optionally mono or di-substituted with a group selected from C1-5 alkyl,
C3-7 cycloalkyl, aryl, arylC1-5alkyl, heterocycl selected from the group
consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl
and indolyl, or heteroaryl selected from the group consisting of furanyl, thienyl,
pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl,
pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl,
benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, halogen,
hydroxy, carboxy and cyano.

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24. The compound according to claim 23 wherein:

Y is O;

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R₁ is C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocycl selected from the group consisting of piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, pyranyl and thiopyranyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl; or amino wherein R₁ is 5 optionally substituted by one or more R_b;

R_b is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocycl selected from the group consisting of pyrrolidinyl, 10 piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 alkoxy, 15 aryloxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl, naphthyl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl and indolinyl, or 20 heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be 25 oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl or aryl, C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, 30 arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, 35 oxo, carboxy, cyano and nitro, R_b may be further optionally substituted by one or more R_c;

R_c is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl, aryl, C1-5 alkoxy, aryloxy, halogen, hydroxy, oxo, carboxy and cyano;

R₂ is H or methyl;

R₃ is H, C1-5 alkyl, C3-7 cycloalkyl or phenyl wherein R₃ is optionally substituted by 40 one or more R_d;

R_d is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocycl selected from the group consisting of piperidinyl, 45 morpholinyl and piperazinyl, heteroaryl selected from the group consisting of

furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl,
 benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and
 isoquinolinyl, C1-5 alkoxy, aryloxy, aroyl, C1-5 alkoxy carbonyl,
 aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen
 atom may be independently mono or di-substituted by C1-5 alkyl, aryl,
 heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl,
 morpholinyl and piperazinyl or heteroaryl selected from the group consisting of
 furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl,
 benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and
 isoquinolinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur
 atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom
 may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom
 may be independently substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl
 selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or
 heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,
 thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl,
 benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5
 alkoxy carbonylamino, aryloxycarbonylamino, C1-5 alkyl carbamoyloxy,
 aryl carbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5
 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be
 independently mono or di-substituted by C1-5 alkyl, phenyl, naphthyl,
 heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and
 piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl,
 pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl,
 benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl,
 halogen, hydroxy, oxo, carboxy and cyano, R_d may be further optionally
 substituted by one or more R_e;

R_e is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl,
 30 aryl, arylC1-5alkyl, C1-5 alkoxy, aryloxy, arylC1-3alkoxy, aroyl, amino,
 halogen, hydroxy, oxo, carboxy and cyano;

R₄ is H or methyl;

35 R₅ is H or C1-5 alkyl;
 R₅ is H or C1-5 alkyl;

R₆ is H, C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl or cyano, wherein R₆ is optionally
 40 substituted by one or more R_f.

R_f is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, phenyl,
 naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl,
 piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl
 45 selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,
 thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl,

indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalanyl, C1-5 alkoxy, aryloxy, arylC1-Salkoxy, heteroarylC1-5alkoxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be
5 independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylC1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be
10 independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5
15 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy and cyano, R_f may be further optionally substituted by one or more R_g;
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30 R_g is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, phenyl optionally substituted by one or more groups selected from halogen, methyl or methoxy, naphthyl optionally substituted by one or more groups selected from halogen, methyl or methoxy, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalanyl, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl,
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benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino,
5 aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a
sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a
sulfoxide or sulfone, ureido wherein either nitrogen atom may be
independently substituted by C1-5 alkyl, aryl, heterocycl selected from
the group consisting of piperidinyl, morpholinyl and piperazinyl or
heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl,
oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl,
benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl,
10 C1-5 alkoxy carbonylamino, aryloxy carbonylamino, C1-5
alkyl carbamoyloxy, aryl carbamoyloxy, C1-5 alkylsulfonylamino,
arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino
wherein the nitrogen atom may be independently mono or di-substituted
by C1-5 alkyl, aryl, heterocycl selected from the group consisting of
15 pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl or heteroaryl
selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,
thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl,
benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, halogen,
hydroxy, oxo, carboxy and cyano;

20

R_h is selected from the group consisting of C1-5 alkyl, phenyl, naphthyl, C1-5
25 alkoxy carbonyl, aryloxy carbonyl, aryl C1-3 alkoxy carbonyl, carbamoyl wherein
the nitrogen atom may be optionally mono or di-substituted with a group selected
from C1-5 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, aryl C1-3 alkyl, heterocycl
selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and
piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl,
30 pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl,
benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl,
halogen, hydroxy, carboxy and cyano; and

X is O.

35

25. The compound according to claim 24 wherein:

40

Y is O;

R₁ is C1-5 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocycl selected from the group
45 consisting of piperidinyl, morpholinyl, piperazinyl, pyranyl and thiopyranyl; heteroaryl
selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl,

imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl or amino, wherein R₁ is optionally substituted by one or more R_b;

- 5 R_b is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-3 alkoxy, phenoxy, C1-3 alkoxy carbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, phenyl or naphthyl; C1-5 alkoxy carbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy and cyano, R_b may be further optionally substituted by one or more R_c;
- 10 20 25
- 30 R_c is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, aryl, C1-3 alkoxy, phenoxy, halogen, hydroxy, oxo, carboxy and cyano;
- 35 R₂ is H;
- 40 R₃ is C1-5 alkyl, C3-6 cycloalkyl or phenyl, wherein R₃ is optionally substituted by one or more R_d;
- 45 R_d is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, quinolinyl and isoquinolinyl, C1-5 alkoxy, phenoxy, aroyl, C1-5 alkoxy carbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl,

morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, C1-5 alkanoylamino, aroylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, phenylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-3 alkyl, phenyl or heteroaryl selected the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, C1-5 alkoxy carbonylamino, C1-5 alkyl carbamoyloxy, aryl carbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, phenyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, halogen, hydroxy, oxo, carboxy and cyano, R_d may be further optionally substituted by one or more R_e;

R_e is selected from the group consisting of C1-5 alkyl, C5-6 cycloalkyl, phenyl, naphthyl, arylC1-3alkyl, C1-5 alkoxy, phenoxy, arylC1-3alkoxy, aroyl, amino, halogen, hydroxy, oxo, carboxy and cyano;

20

R₄ is H;

R₆ is H, C1-5 alkyl, C3-6 cycloalkyl, phenyl or cyano, wherein R₆ is optionally substituted by one or more R_f;

R_f is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 alkoxy, aryloxy, arylC1-3alkoxy, heteroarylC1-3alkoxy, C1-5 alkoxy carbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, C1-5 alkanoylamino, aroylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylC1-3alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl or phenyl, C1-5 alkoxy carbonylamino, C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, halogen, hydroxy,

oxo, carboxy and cyano, R_f may be further optionally substituted by one or more R_g;

5 R_g is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl optionally substituted by one or more groups selected from halogen or methyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, pyrimidinyl, pyrazinyl and indolyl, C1-5 alkoxy, aryloxy, arylC1-3alkoxy, C1-5 alkoxy carbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or aryl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl or aryl, C1-5 alkoxy carbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or aryl, halogen, hydroxy, oxo, carboxy and cyano;

10

15

20

25 R_h is selected from the group consisting of C1-5 alkyl, phenyl, C1-5 alkoxy carbonyl, aryloxycarbonyl, arylC1-3alkoxy carbonyl, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with C1-5 alkyl, C3-6 cycloalkyl, phenyl, naphthyl or arylC1-3alkyl; halogen, hydroxy, carboxy and cyano.

30

26. The compound according to claim 25 wherein:

35 R₁ is C1-3 alkyl, C5-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl, piperazinyl, pyranyl and thiopyranyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl or amino, wherein R₁ is optionally substituted by one or more R_b;

40

45 R_b is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-3 alkoxy, C1-3

alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, phenyl or heteroaryl selected from the group consisting of pyrrolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl and benzthiazolyl 5 C1-5 alkanoylamino, aroylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-3alkyl or phenyl, C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3alkyl, phenyl, heterocyclyl selected 10 from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of pyrrolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy and cyano, R_b may be further 15 optionally substituted by one or more R_c;

R_c is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, C1-3 alkoxy, halogen and hydroxy;

20 R₃ is C1-5 alkyl, C5-6 cycloalkyl or phenyl wherein R₃ is optionally substituted by one or more R_d;

25 R_d is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, 4-piperidinyl, 4-morpholinyl, piperazinyl, furanyl, thieryl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-5 alkoxy, phenoxy, aroyl, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or phenyl, C1-5 alkanoylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-3 alkyl or phenyl, C1-5 alkoxycarbonylamino, C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, halogen, hydroxy, oxo, carboxy and cyano, R_d may be further optionally substituted by one or more R_e; 30

35 R_e is selected from the group consisting of C1-5 alkyl, C5-6 cycloalkyl, phenyl, benzyl, C1-5 alkoxy, phenoxy, benzyloxy, aroyl, halogen, hydroxy, oxo, carboxy and cyano;

40 R₅ is H or C1-3alkyl;

R₆ is H, C1-5 alkyl, phenyl or cyano, wherein R₆ is optionally substituted by one or more R_f;

45 R_f is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, furanyl, thieryl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-3 alkoxy,

benzyloxy, pyridylC1-3alkoxy, thietylC1-3alkoxy, furanylC1-3alkoxy, C1-3
5 alkoxy carbonyl, phenoxyoxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl
wherein the nitrogen atom may be independently mono or di-substituted by C1-3
alkyl or phenyl, C1-5 alkanoylamino, aroylamino, methylthio wherein the sulfur
atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur
10 atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen
atom may be independently substituted by C1-5 alkyl or phenyl, C1-3
alkoxycarbonylamino, amino wherein the nitrogen atom may be independently
mono or di-substituted by C1-5 alkyl or phenyl, halogen, hydroxy, oxo, carboxy
and cyano, R_f may be further optionally substituted by one or more R_g;

15 R_g is selected from the group consisting of C1-3 alkyl, phenyl optionally
substituted by one or more groups selected from the group consisting of
halogen and methyl, heterocyclyl selected from the group consisting of
piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the
group consisting of furanyl, thietyl, pyrrolyl and pyridinyl, C1-3 alkoxy,
aryloxy, benzyloxy, C1-5 alkoxy carbonyl, C1-5 alkanoyloxy, aroyloxy,
20 carbamoyl wherein the nitrogen atom may be independently mono or di-
substituted by C1-5 alkyl or phenyl, C1-5 alkanoylamino, aroylamino, C1-
5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or
sulfone, ureido wherein either nitrogen atom may be independently
substituted by C1-5 alkyl or phenyl, C1-5 alkoxy carbonylamino, C1-5
25 alkylcarbamoyloxy, arylcarbamoyloxy, C1-3 alkylsulfonylamino,
arylsulfonylamino, C1-3 alkylaminosulfonyl, arylaminosulfonyl, amino
wherein the nitrogen atom may be independently mono or di-substituted
by C1-3 alkyl or phenyl, halogen, hydroxy, oxo, carboxy and cyano;

30 R_h is selected from the group consisting of C1-3 alkyl, phenyl, C1-3
alkoxycarbonyl, phenoxyoxycarbonyl, benzyloxy, carbamoyl wherein the
nitrogen atom may be optionally mono or di-substituted with a group selected
from the group consisting of C1-5 alkyl, phenyl and benzyl, halogen, hydroxy,
carboxy and cyano.

35

27. The compound according to claim 26 wherein:

40

R_i is C5-6 cycloalkyl, phenyl, naphthyl, piperidinyl, morpholinyl, piperazinyl, pyranyl,
thiopyranyl, furanyl, thietyl, pyrrolyl or amino, wherein R_i is optionally substituted by
one or more R_b;

45

- R_b is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl, furanyl, thieryl, pyrrolyl, imidazolyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, C1-3 alkoxy, C1-3 alkoxy carbonyl, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; C1-5
5 alkanoylamino, aroylamino, ureido wherein either nitrogen atom may be independently substituted by C1-3 alkyl or phenyl; C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, halogen, hydroxy, oxo, carboxy and cyano, R_b may be further optionally substituted by one or more R_c;
- 10 R_c is selected from the group consisting of C1-3 alkyl, C1-3 alkoxy, halogen and hydroxy;
- 15 R₃ is C1-5 alkyl, C5-6 cycloalkyl or phenyl, wherein R₃ is optionally substituted by one or more groups of the formula R_d;
R_d is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, 4-piperidinyl, furanyl, thieryl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-3 alkoxy, C1-5
20 alkoxy carbonyl, C1-5 alkanoyloxy, benzoyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, C1-5 alkanoylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, C1-3 alkoxy carbonylamino, C1-3 alkylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, halogen, hydroxy, oxo, carboxy and cyano, R_d may be further optionally substituted by one or more R_e;
- 25 R_e is selected from the group consisting of C1-3 alkyl, phenyl, benzyl, C1-3 alkoxy, phenoxy, benzyloxy, benzoyl, halogen, hydroxy, oxo, carboxy and cyano;
wherein the configuration at the stereocenter defined by R₂ and R₃ and the carbon they are attached to is defined as L;
- 30 R₅ is H or methyl;
- 35 R₆ is C1-5 alkyl, phenyl or cyano wherein R₆ is optionally substituted by one or more groups of the formula R_f;
R_f is selected from the group consisting of methyl, C3-6 cycloalkyl, phenyl, naphthyl, furanyl, thieryl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-3 alkoxy, benzyloxy, pyridyl C1-3 alkoxy, thieryl C1-3 alkoxy, furanyl C1-3 alkoxy, C1-5
40 alkanoylamino, aroylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, C1-3 alkoxy carbonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or phenyl, halogen, hydroxy, oxo, carboxy and cyano, R_f may be further optionally substituted by one or more R_g;
- 45

5 R_g is selected from the group consisting of C1-3 alkyl, phenyl optionally substituted by one or more groups selected from halogen or methyl, C1-3 alkoxy, aryloxy, benzyloxy, C1-3 alkoxycarbonyl, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, C1-5 alkanoylamino, arylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, halogen, hydroxy, oxo, carboxy and cyano;

10 R_h is selected from the group consisting of C1-3 alkyl, phenyl, C1-3 alkoxycarbonyl, benzyloxy and carboxy.

15 28. The compound according to claim 27 wherein:

20 R₁ is cyclohexyl, phenyl, naphthyl, piperidinyl, morpholinyl, piperazinyl, pyranyl, thiopyranyl or amino wherein R₁ is optionally substituted by one or more R_b;

25 R_b is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl, furanyl, thienyl, pyrrolyl, imidazolyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, C1-3 alkoxy, C1-3 alkoxycarbonyl, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, C1-5 alkanoylamino, arylamino, C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, halogen, hydroxy, oxo, carboxy and cyano, R_b may be further optionally substituted by one or more R_c;

30 R_c is selected from the group consisting of C1-3 alkoxy, halogen and hydroxy,

35 R₃ is C1-5 alkyl or C5-6 cycloalkyl wherein R₃ is optionally substituted by one or more R_d;

40 R_d is selected from the group consisting of methyl, C3-6 cycloalkyl, phenyl, naphthyl, thienyl, imidazolyl, pyridinyl, indolyl, C1-4 alkoxy, C1-5 alkanoylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, halogen, hydroxy, oxo, carboxy and cyano, R_d may be further optionally substituted by one or more R_e;

45 R_e is selected from the group consisting of methyl, phenyl, benzyl, methoxy, phenoxy, benzyloxy, benzoyl, halogen and hydroxy;

R₆ is C1-5 alkyl or phenyl, wherein R₆ is optionally substituted by one or more R_f;

5 R_f is selected from the group consisting of C3-6 cycloalkyl, phenyl, naphthyl, thienyl, imidazolyl, pyridinyl, indolyl, methoxy, benzyloxy, C1-3 alkanoylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, methoxycarbonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, halogen, hydroxy, carboxy and cyano, R_f may be further optionally substituted by one or more R_g;

10 R_g is selected from the group consisting of methyl, phenyl optionally substituted by one or more groups selected from halogen or methyl, methoxy, phenoxy, benzyloxy, methoxycarbonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, halogen, hydroxy and carboxy;

15

20 R_h is selected from the group consisting of vinyl, phenyl, methoxycarbonyl, benzyloxycarbonyl and carboxy;

25 29. The compound according to claim 28 wherein:

30 R₁ is cyclohexyl, phenyl, naphthyl, piperidinyl, morpholinyl, piperazinyl, pyranyl or thiopyranyl, wherein R₁ is optionally substituted by one or more R_b;

35 R_b is selected from the group consisting of pyrrolyl, imidazolyl, indolyl, benzimidazolyl, methoxy, methoxycarbonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, halogen, hydroxy and carboxy, R_b may be further optionally substituted by one or more R_c;

40 R_c is selected from the group consisting of methoxy, halogen and hydroxy;

45 R_d is selected from the group consisting of methyl, C3-6 cycloalkyl, phenyl, naphthyl, C1-4 alkoxy, C1-3 alkanoylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, halogen, hydroxy, oxo, carboxy and cyano, R_d may be further optionally substituted by one or more R_e;

R_e is selected from the group consisting of methyl, phenyl, methoxy, halogen and hydroxy;

R₅ is H;

45

5 R_f is selected from the group consisting of C5-6 cycloalkyl, phenyl, naphthyl, thieryl, indolyl, methoxy, benzyloxy, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, methoxycarbonylamino, halogen, hydroxy, carboxy and cyano, R_f may be further optionally substituted by one or more R_g;

10 R_g is selected from the group consisting of methyl, phenyl optionally substituted by halogen, methoxy, phenoxy, benzyloxy, methoxycarbonyl, halogen, hydroxy and carboxy;

15 R_h is vinyl or phenyl.

15

30. The compound according to claim 29 wherein:

20 R₁ is phenyl, naphthyl or 4-morpholinyl wherein R₁ is optionally substituted by one or more R_b;

25 R_b is selected from the group consisting of benzimidazolyl, methoxy and dimethylamino R_b may be further optionally substituted by R_c wherein R_c is a halogen atom;

30 R₃ is C1-5 alkyl wherein R₃ is optionally substituted by one or more R_d;

35 R_d is selected from the group consisting of C3-6 cycloalkyl, phenyl or naphthyl, R_d may be further optionally substituted by one or more R_e;

40 R_e is selected from the group consisting of methyl and halogen,

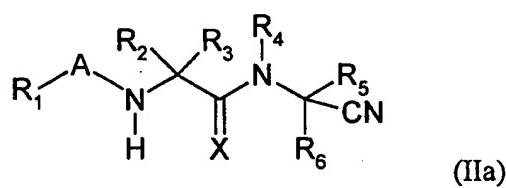
45 R_f is selected from the group consisting of C5-6 cycloalkyl, phenyl, naphthyl, indolyl, benzyloxy, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, halogen and carboxy, R_f may be further optionally substituted by one or more R_g;

50 R_g is selected from the group consisting of methyl, methoxy, methoxycarbonyl, halogen and hydroxy.

55

31. A compound of the formula (IIa):

5



10

wherein:

A is -C(Y)- or -SO₂-

15

Y is O, S or NR_a wherein R_a is selected from the group consisting of H, alkyl, aryl, alkoxy, aryloxy, alkylamino and arylamino;

20

R₁ is alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl or amino wherein R₁ is optionally substituted by one or more R_b;

25

R_b is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkoxy, aryloxy, alkanoyl, aroyl, alkoxy carbonyl, aryloxycarbonyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkoxy carbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino; R_b may be further optionally substituted by one or more R_c;

35

R_c is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, arylalkyl, alkoxy, aryloxy, arylalkoxy, alkanoyl, aroyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

40

R₂ is H or alkyl;

5 R₃ is H, C₂-8alkyl, cycloalkyl, aryl, heterocyclyl or heteroaryl, wherein R₃ is optionally substituted by one or more R_d;

10 R_d is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkoxy, aryloxy, arylalkoxy, alkoxycarbonyl, aryloxycarbonyl, alkanoyl, aroyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkanoylamino, aroylamino, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkoxycarbonylamino, 15 aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R_d may be further optionally substituted by one or 20 more R_e;

25 R_e is selected from the group consisting of alkyl, cycloalkyl, aryl, arylalkyl, alkoxy, aryloxy, arylalkoxy, alkanoyl, aroyl, amino, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

30 R₄ is H or alkyl;

30 R₅ is H or alkyl;

35 R₆ is H, alkyl, cycloalkyl, aryl, heterocyclyl, aryl, heteroaryl or cyano, wherein R₆ is optionally substituted by one or more R_f;

40 R_f is selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkoxy, aryloxy, arylalkoxy, alkanoyl, aroyl, alkoxycarbonyl, aryloxycarbonyl, alkanoyloxy, aroyloxy, heteroarylalkoxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkanoylamino, aroylamino, alkylcarbamoyl, 45 arylcarbamoyl, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylalkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkoxycarbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy,

alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R_f may be further optionally substituted by one or more R_g;

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R_g is selected from the group consisting of alkyl, cycloalkyl, aryl optionally substituted by one or more groups selected from halogen, methyl or methoxy, heterocyclyl, heteroaryl, alkoxy, aryloxy, arylalkoxy, alkoxycarbonyl, aryloxycarbonyl, alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkanoylamino, aroylamino, alkylcarbamoyl, arylcarbamoyl, alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl or heteroaryl, alkoxycarbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

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or R₅ and R₆ together with the carbon they are attached form a carbocyclic ring of 3 to 6 carbon atoms, the carbocyclic ring being optionally substituted with one or more R_h;

R_h is selected from the group consisting of alkyl, aryl, alkoxycarbonyl, aryloxycarbonyl, arylalkoxycarbonyl, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with a group selected from alkyl, cycloalkyl, aryl, arylalkyl, heterocyclyl, heteroaryl, halogen, hydroxy, carboxy and cyano;

X is O, S or N-OH;

35

and the pharmaceutically acceptable derivatives thereof;

with the following provisos:

40

when Y is O and R₆ is arylalkyl or heteroarylalkyl then R₁ cannot be alkyl, cycloalkyl, aryl, heteroaryl, cycloalkyl-alkyl, aryl-alkyl or aryl-cycloalkyl;

when R₅ is H then R₆ cannot be H;
and

45

when R₁ is C1alkyl then R_b cannot be carbamoyl, alkanoylamino, aroylamino, ureido, alkoxy carbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, amino, amidino or guanidino wherein each said R_b is linked to said R₁ via the nitrogen atom thereof.

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32. The compound according to claim 31 wherein:

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Y is O, S or NR_a wherein R_a is H, alkyl or aryl;

R₁ is C1-8alkyl, C3-7cycloalkyl, aryl, heterocyclyl selected from the group consisting of 15 pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, indolinyl, pyranlyl and thiopyranlyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl, phenoxazinyl, and amino wherein R₁ is optionally substituted by one or more R_b;

R_b is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, 25 pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, 30 quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl or phenoxazinyl, C1-8 alkoxy, aryloxy, C1-8 alkoxy carbonyl, aryloxycarbonyl, C1-8 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, 35 pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, 40 quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkanoylamino, aroylamino, C1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected 45 from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl,

- imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl or phenoxazinyl, alkoxycarbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thieryl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, pyrazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoxazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino, guanidino; R_b may be further optionally substituted by one or more R_c;
- R_c is selected from the group consisting of C1-8 alkyl, C3-6 cycloalkyl, aryl, C1-8 alkoxy, aryloxy, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;
- 25 R₃ is H, C2-8 alkyl, C3-7 cycloalkyl, aryl wherein R₃ is optionally substituted by one or more R_d;
- R_d is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thieryl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkoxy, aryloxy, alkanoyl, aroyl, C1-8 alkoxycarbonyl, aryloxycarbonyl, C1-8 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thieryl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxaliny, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkanoylamino, aroylamino, C1-8 alkylthio wherein the sulfur atom may be

oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be
5 oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be
independently substituted by alkyl, aryl, heterocyclyl selected from the group
consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl
10 and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl,
pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl,
oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl,
15 pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl,
benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl,
carbazolyl, phenothiazinyl and phenoxazinyl, alkoxycarbonylamino,
aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy,
alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl,
20 amino wherein the nitrogen atom may be independently mono or di-substituted by
alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl,
piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl
selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,
thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl,
25 tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl,
isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl,
quonolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl
and phenoxazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino,
guanidino, R_d may be further optionally substituted by one or more R_e;

25 R_e is selected from the group consisting of C1-8 alkyl, C3-6 cycloalkyl,
aryl, arylalkyl, C1-8 alkoxy, aryloxy, arylalkoxy, aroyl, amino, halogen,
hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

30 R₆ is H, C1-8 alkyl, C3-7 cycloalkyl, aryl or cyano, wherein R₆ is optionally substituted
by one or more R_f;

35 R_f is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, aryl,
heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl,
morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from
the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl,
pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl,
40 pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl,
benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl,
quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8
alkoxy, aryloxy, arylC1-8alkoxy, heteroarylC1-8alkoxy, C1-8 alkoxycarbonyl,
aryloxycarbonyl, C1-8 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen
atom may be independently mono or di-substituted by C1-8 alkyl, aryl,
45 heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl,
morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected
from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl,
imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl,

thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxyazinyl, C1-8 alkanoylamino, aroylamino, C1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, 5 piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxyazinyl, alkoxy carbonylamino, aryloxy carbonylamino, alkyl carbamoyloxy, aryl carbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, 10 piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, 15 quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxyazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R_f may be further optionally substituted by one or more R_g;

R_g is selected from the group consisting of C1-8 alkyl, C3-7 cycloalkyl, 30 aryl optionally substituted by one or more groups selected from halogen, methyl or methoxy, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxyazinyl, C1-8 alkoxy, aryloxy, aryl C1-8 alkoxy, C1-8 35 alkoxy carbonyl, aryloxy carbonyl, C1-8 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl,

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pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, C1-8 alkanoylamino, aroylamino, C1-8 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, alkoxy carbonylamino, aryloxy carbonylamino, alkyl carbamoyloxy, aryl carbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino, and guanidino;

30 or R₅ and R₆ together with the carbon they are attached form a carbocyclic ring of 3 to 6 carbon atoms, the carbocyclic ring being optionally substituted with one or more R_h;

R_h is selected from the group consisting of C1-8 alkyl, aryl, C1-8 alkoxy carbonyl, aryloxy carbonyl, aryl C1-8 alkoxy carbonyl, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with a group selected from C1-8 alkyl, C3-7 cycloalkyl, aryl, aryl C1-8 alkyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, carbazolyl, phenothiazinyl and phenoxazinyl, halogen, hydroxy, carboxy, cyano; and

45 X is O or S.

5 33. The compound according to claim 32 wherein:

Y is O or S;

10 R₁ is C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, indolinyl, pyranyl and thiopyranyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl or amino; wherein R₁ is optionally substituted by one or more R_b;

20 R_b is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxy, aryloxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-8 alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl,

or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R_b may be further optionally substituted by one or more R_c;

R_c is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl, aryl, C1-5 alkoxy, aryloxy, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

R₂ is H or C1-3 alkyl;

R₃ is H, C2-5 alkyl, C3-7 cycloalkyl, aryl wherein R₃ is optionally substituted by one or more R_d;

R_d is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, aryl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny, C1-5 alkoxy, aryloxy, C1-5 alkanoyl, aroyl, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny, C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl,

5 pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R_d may be further optionally substituted by one or more R_e;

10 R_e is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl, aryl, arylalkyl, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, aroyl, amino, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

15 R₄ is H or C1-3 alkyl

20 R₅ is H or C1-8 alkyl

25 R₆ is H, C1-5 alkyl, C3-7 cycloalkyl, aryl or cyano, wherein R₆ is optionally substituted by one or more R_f;

30 R_f is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, aryl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, heteroarylC1-5alkoxy, C1-5 alkoxy carbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxaliny, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylC1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and

quinoxaliny, C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, 5 aryl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinoliny, 10 isoquinoliny, quinazolinyl and quinoxaliny, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino, R_f may be further optionally substituted by one or more R_g;

15 R_g is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, aryl optionally substituted by one or more groups selected from halogen, methyl or methoxy, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, 20 pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinoliny, isoquinoliny, quinazolinyl and quinoxaliny, C1-5 alkoxy, aryloxy, arylC1-5alkoxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl or heteroaryl selected from the group consisting of furanyl, 25 thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinoliny, isoquinoliny, quinazolinyl and quinoxaliny, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, aryl, 30 heterocycl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinoliny, isoquinoliny, quinazolinyl and quinoxaliny, 35 C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, heterocycl selected from the group consisting of 40 pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and 45

indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino;

or R₅ and R₆ together with the carbon they are attached form a carbocyclic ring of 3 to 6 carbon atoms, the carbocyclic ring being optionally substituted with one or more R₈:

10 R_h is selected from the group consisting of C1-5 alkyl, aryl, C1-5 alkoxycarbonyl,
aryloxycarbonyl, arylC1-5alkoxycarbonyl, carbamoyl wherein the nitrogen atom
may be optionally mono or di-substituted with a group selected from C1-5 alkyl,
C3-7 cycloalkyl, aryl, arylC1-5alkyl, heterocyclyl selected from the group
15 consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl
and indolinyl, or heteroaryl selected from the group consisting of furanyl, thieryl,
pyrrolyl, oxazolyl, thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl,
pyrimidinyl, pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl,
benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl, halogen,
20 hydroxy, carboxy and cyano.

34. The compound according to claim 33 wherein:

Y is Q.

30 R₁ is C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, pyranyl and thiopyranyl; heteroaryl selected from the group consisting of furanyl, thieryl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl; or amino wherein R₁ is optionally substituted by one or more R₈:

40 R_b is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 alkoxy, aryloxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-
45 substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl and indolinyl, or

heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by alkyl or aryl, C1-5 alkoxy carbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, 5 arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by alkyl, aryl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl, or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, 10 oxo, carboxy, cyano and nitro, R_b may be further optionally substituted by one or more R_c;

20 R_c is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl, aryl, C1-5 alkoxy, aryloxy, halogen, hydroxy, oxo, carboxy and cyano;

R₂ is H or methyl;

25 R₃ is H, C2-5 alkyl, C3-7 cycloalkyl or phenyl wherein R₃ is optionally substituted by one or more R_d;

30 R_d is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 alkoxy, aryloxy, aroyl, C1-5 alkoxy carbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, aryl, 35 heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or 40 heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 45

alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, 5
arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5
alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be
independently mono or di-substituted by C1-5 alkyl, phenyl, naphthyl,
heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and
piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl,
pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl,
benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl,
halogen, hydroxy, oxo, carboxy and cyano, R_d may be further optionally
10 substituted by one or more R_e;

R_e is selected from the group consisting of C1-5 alkyl, C3-6 cycloalkyl,
aryl, arylC1-5alkyl, C1-5 alkoxy, aryloxy, arylC1-3alkoxy, aroyl, amino,
halogen, hydroxy, oxo, carboxy and cyano;

15 R₄ is H or methyl;

20 R₅ is H or C1-5 alkyl;

R₆ is H, C1-5 alkyl, C3-7 cycloalkyl, phenyl, naphthyl or cyano, wherein R₆ is optionally
substituted by one or more R_f;

25 R_f is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl, phenyl,
naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl,
piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl
selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,
thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl, pyrazinyl,
30 indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl,
isoquinolinyl, quinazolinyl and quinoxalinyl, C1-5 alkoxy, aryloxy, arylC1-
5alkoxy, heteroarylC1-5alkoxy, C1-5 alkoxy carbonyl, aryloxycarbonyl, C1-5
alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be
independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected
35 from the group consisting of piperidinyl, morpholinyl and piperazinyl or
heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl,
oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl,
benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino,
40 aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a
sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a
sulfoxide or sulfone, arylC1-5 alkylthio wherein the sulfur atom may be oxidized
to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be
independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from the
group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl
45 selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,
thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl,

benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5
alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy,
arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5
alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be
5 independently mono or di-substituted by C1-5 alkyl, aryl, heterocyclyl selected
from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and
piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl,
pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl,
10 benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl,
halogen, hydroxy, oxo, carboxy and cyano, R_f may be further optionally
substituted by one or more R_g;

R_g is selected from the group consisting of C1-5 alkyl, C3-7 cycloalkyl,
15 phenyl optionally substituted by one or more groups selected from
halogen, methyl or methoxy, naphthyl optionally substituted by one or
more groups selected from halogen, methyl or methoxy, heterocyclyl
selected from the group consisting of pyrrolidinyl, piperidinyl,
morpholinyl, thiomorpholinyl, piperazinyl and indolinyl; heteroaryl
selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,
20 thiazolyl, imidazolyl, triazolyl, tetrazolyl, pyridinyl, pyrimidinyl,
pyrazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl,
benzthiazolyl, quinolinyl, isoquinolinyl, quinazolinyl and quinoxalinyl,
C1-5 alkoxy, aryloxy, arylC1-5alkoxy, C1-5 alkoxycarbonyl,
aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the
25 nitrogen atom may be independently mono or di-substituted by C1-5 alkyl,
aryl, heterocyclyl selected from the group consisting of piperidinyl,
morpholinyl and piperazinyl or heteroaryl selected from the group
consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl,
30 pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl,
benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino,
arylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a
sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a
35 sulfoxide or sulfone, ureido wherein either nitrogen atom may be
independently substituted by C1-5 alkyl, aryl, heterocyclyl selected from
the group consisting of piperidinyl, morpholinyl and piperazinyl or
heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl,
oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl,
40 benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl,
C1-5 alkoxycarbonylamino, aryloxycarbonylamino, C1-5
alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino,
arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino
wherein the nitrogen atom may be independently mono or di-substituted
45 by C1-5 alkyl, aryl, heterocyclyl selected from the group consisting of
pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl or heteroaryl
selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,
thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl,

benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, oxo, carboxy and cyano;

5 or R₅ and R₆ together with the carbon they are attached form a carbocyclic ring of 3 to 6 carbon atoms, the carbocyclic ring being optionally substituted with one or more R_h;

R_h is selected from the group consisting of C1-5 alkyl, phenyl, naphthyl, C1-5 alkoxy carbonyl, aryloxy carbonyl, aryl C1-3 alkoxy carbonyl, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with a group selected from C1-5 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, aryl C1-3 alkyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy, carboxy and cyano; and

X is O.

20

35. The compound according to claim 34 wherein:

25

Y is O;

R₁ is C1-5 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl, piperazinyl, pyranyl and thiopyran; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl or amino, wherein R₁ is optionally substituted by one or more R_b;

35

R_b is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-3 alkoxy, phenoxy, C1-3 alkoxy carbonyl, aryloxy carbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be

oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be
oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be
independently substituted by C1-5alkyl, phenyl or naphthyl; C1-5
5 alkoxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5
alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl,
arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono
or di-substituted by C1-5alkyl, phenyl, naphthyl, heterocyclyl selected from the
group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl
selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl,
10 thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl,
benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, halogen, hydroxy,
oxo, carboxy and cyano, R_b may be further optionally substituted by one or more
R_c;

15 R_c is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl,
aryl, C1-3 alkoxy, phenoxy, halogen, hydroxy, oxo, carboxy and cyano;

R₂ is H;

20 R₃ is C2-5 alkyl, C3-6 cycloalkyl or phenyl, wherein R₃ is optionally substituted by one
or more R_d;

25 R_d is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl,
naphthyl, heterocyclyl selected from the group consisting of piperidinyl,
morpholinyl and piperazinyl; heteroaryl selected from the group consisting of
furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, quinolinyl and
isoquinolinyl, C1-5 alkoxy, phenoxy, aroyl, C1-5 alkoxycarbonyl,
aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen
atom may be independently mono or di-substituted by C1-5 alkyl, phenyl,
30 naphthyl, heterocyclyl selected from the group consisting of piperidinyl,
morpholinyl and piperazinyl or heteroaryl selected from the group consisting of
furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl,
C1-5 alkanoylamino, aroylamino, C1-3 alkylthio wherein the sulfur atom may be
oxidized to a sulfoxide or sulfone, phenylthio wherein the sulfur atom may be
35 oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be
independently substituted by C1-3 alkyl, phenyl or heteroaryl selected the group
consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl
and indolyl, C1-5 alkoxycarbonylamino, C1-5 alkylcarbamoyloxy,
arylcaramoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein
40 the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl,
phenyl, heterocyclyl selected from the group consisting of piperidinyl,
morpholinyl and piperazinyl or heteroaryl selected from the group consisting of
furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl,
halogen, hydroxy, oxo, carboxy and cyano, R_d may be further optionally
45 substituted by one or more R_e;

R_e is selected from the group consisting of C1-5 alkyl, C5-6 cycloalkyl, phenyl, naphthyl, arylC1-3alkyl, C1-5 alkoxy, phenoxy, arylC1-3alkoxy, aroyl, amino, halogen, hydroxy, oxo, carboxy and cyano;

5

R₄ is H;

R₆ is H, C1-5 alkyl, C3-6 cycloalkyl, phenyl or cyano, wherein R₆ is optionally substituted by one or more R_f;

10

R_f is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-5 alkoxy, aryloxy, arylC1-3alkoxy, heteroarylC1-3alkoxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl, C1-5 alkanoylamino, aroylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylC1-3alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl or phenyl, C1-5 alkoxycarbonylamino, C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, indolyl, halogen, hydroxy, oxo, carboxy and cyano, R_f may be further optionally substituted by one or more R_g;

35

R_g is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl optionally substituted by one or more groups selected from halogen or methyl, heterocyclyl selected from the group consisting of pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl, heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl, pyrimidinyl, pyrazinyl and indolyl, C1-5 alkoxy, aryloxy, arylC1-3alkoxy, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or aryl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl or aryl, C1-5

40

45

alkoxycarbonylamino, aryloxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-5 alkylsulfonylamino, arylsulfonylamino, C1-5 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or aryl, halogen, hydroxy, oxo, carboxy and cyano;

5

or R₅ and R₆ together with the carbon they are attached form a carbocyclic ring of 3 to 6 carbon atoms, the carbocyclic ring being optionally substituted with one or more R_h;

10

R_h is selected from the group consisting of C1-5 alkyl, phenyl, C1-5 alkoxycarbonyl, aryloxycarbonyl, arylC1-3alkoxycarbonyl, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with C1-5 alkyl, C3-6 cycloalkyl, phenyl, naphthyl or arylC1-3alkyl; halogen, hydroxy, carboxy and cyano.

15

36. The compound according to claim 35 wherein:

20

R₁ is C1-3 alkyl, C5-6 cycloalkyl, phenyl, naphthyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl, piperazinyl, pyranyl and thiopyranyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyridinyl and indolyl or amino, wherein R₁ is optionally substituted by one or more R_b;

25

R_b is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl, imidazolyl, tetrazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl, C1-3 alkoxy, C1-3 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, phenyl or heteroaryl selected from the group consisting of pyrrolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl and benzthiazolyl C1-5 alkanoylamino, aroylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, arylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-3alkyl or phenyl, C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3alkyl, phenyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl or heteroaryl selected from the group consisting of pyrrolyl, imidazolyl, pyridinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, quinolinyl

40

45

and isoquinolinyl, halogen, hydroxy, oxo, carboxy and cyano, R_b may be further optionally substituted by one or more R_c;

5 R_c is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, C1-3 alkoxy, halogen and hydroxy;

R₃ is C2-5 alkyl, C5-6 cycloalkyl or phenyl wherein R₃ is optionally substituted by one or more R_d;

10 R_d is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, 4-piperidinyl, 4-morpholinyl, piperazinyl, furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-5 alkoxy, phenoxy, aroyl, C1-5 alkoxycarbonyl, aryloxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or phenyl, C1-5
15 alkanoylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-3 alkyl or phenyl, C1-5 alkoxycarbonylamino, C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, halogen, hydroxy,
20 oxo, carboxy and cyano, R_d may be further optionally substituted by one or more R_e;

25 R_e is selected from the group consisting of C1-5 alkyl, C5-6 cycloalkyl, phenyl, benzyl, C1-5 alkoxy, phenoxy, benzyloxy, aroyl, halogen, hydroxy, oxo, carboxy and cyano;

R₅ is H or C1-3alkyl;

30 R₆ is H, C1-5 alkyl, phenyl or cyano, wherein R₆ is optionally substituted by one or more R_f;

35 R_f is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-3 alkoxy, benzyloxy, pyridylC1-3alkoxy, thienylC1-3alkoxy, furanylC1-3alkoxy, C1-3
40 alkoxycarbonyl, phenoxyoxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, C1-5 alkanoylamino, aroylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl or phenyl, C1-3 alkoxycarbonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or phenyl, halogen, hydroxy, oxo, carboxy and cyano, R_f may be further optionally substituted by one or more R_g;

45 R_g is selected from the group consisting of C1-3 alkyl, phenyl optionally substituted by one or more groups selected from the group consisting of

halogen and methyl, heterocyclyl selected from the group consisting of piperidinyl, morpholinyl and piperazinyl; heteroaryl selected from the group consisting of furanyl, thienyl, pyrrolyl and pyridinyl, C1-3 alkoxy, aryloxy, benzyloxy, C1-5 alkoxycarbonyl, C1-5 alkanoyloxy, aroyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or phenyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, ureido wherein either nitrogen atom may be independently substituted by C1-5 alkyl or phenyl, C1-5 alkoxycarbonylamino, C1-5 alkylcarbamoyloxy, arylcarbamoyloxy, C1-3 alkylsulfonylamino, arylsulfonylamino, C1-3 alkylaminosulfonyl, arylaminosulfonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, halogen, hydroxy, oxo, carboxy and cyano;

15 or R₅ and R₆ together with the carbon they are attached form a carbocyclic ring of 3 to 5 carbon atoms, the carbocyclic ring being optionally substituted with one or more R_b;

20 R_b is selected from the group consisting of C1-3 alkyl, phenyl, C1-3 alkoxycarbonyl, phenoxyoxycarbonyl, benzyloxy, carbamoyl wherein the nitrogen atom may be optionally mono or di-substituted with a group selected from the group consisting of C1-5 alkyl, phenyl and benzyl, halogen, hydroxy, carboxy and cyano.

25

37. The compound according to claim 36 wherein:

30 R₁ is C5-6 cycloalkyl, phenyl, naphthyl, piperidinyl, morpholinyl, piperazinyl, pyranyl, thiopyranyl, furanyl, thienyl, pyrrolyl or amino, wherein R₁ is optionally substituted by one or more R_b;

35 R_b is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl, furanyl, thienyl, pyrrolyl, imidazolyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, C1-3 alkoxy, C1-3 alkoxycarbonyl, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl; C1-5 alkanoylamino, aroylamino, ureido wherein either nitrogen atom may be independently substituted by C1-3alkyl or phenyl;, C1-5 alkylsulfonylamino, arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3alkyl or phenyl, halogen, hydroxy, oxo, carboxy and cyano, R_b may be further optionally substituted by one or more R_c;

40 R_c is selected from the group consisting of C1-3alkyl, C1-3alkoxy, halogen and hydroxy;

45

- R₃ is C2-5 alkyl, C5-6 cycloalkyl or phenyl, wherein R₃ is optionally substituted by one or more groups of the formula R_d;
- R_d is selected from the group consisting of C1-3 alkyl, C3-6 cycloalkyl, phenyl, naphthyl, 4-piperidinyl, furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-3 alkoxy, C1-5 alkoxycarbonyl, C1-5 alkanoyloxy, benzyloxy, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, C1-5 alkanoylamino, C1-3 alkylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, C1-3 alkoxycarbonylamino, C1-3 alkylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl,
- 10 halogen, hydroxy, oxo, carboxy and cyano, R_d may be further optionally substituted by one or more R_e;
- R_e is selected from the group consisting of C1-3 alkyl, phenyl, benzyl, C1-3 alkoxy, phenoxy, benzyloxy, benzoyl, halogen, hydroxy, oxo, carboxy and cyano;
- 15 wherein the configuration at the stereocenter defined by R₂ and R₃ and the carbon they are attached to is defined as L;
- R₅ is H or methyl;
- 20 R₆ is C1-5 alkyl, phenyl or cyano wherein R₆ is optionally substituted by one or more groups of the formula R_f;
- R_f is selected from the group consisting of methyl, C3-6 cycloalkyl, phenyl, naphthyl, furanyl, thienyl, thiazolyl, imidazolyl, pyridinyl, indolyl, C1-3 alkoxy, 25 benzyloxy, pyridylC1-3alkoxy, thienylC1-3alkoxy, furanylC1-3alkoxy, C1-5 alkanoylamino, aroylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, C1-3 alkoxycarbonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-5 alkyl or phenyl,
- 30 halogen, hydroxy, oxo, carboxy and cyano, R_f may be further optionally substituted by one or more R_g:
- R_g is selected from the group consisting of C1-3 alkyl, phenyl optionally substituted by one or more groups selected from halogen or methyl, C1-3 alkoxy, aryloxy, benzyloxy, C1-3 alkoxycarbonyl, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, C1-5 alkanoylamino, aroylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, halogen, hydroxy, oxo, carboxy and cyano;
- 35 or R₅ and R₆ together with the carbon they are attached form a carbocyclic ring of 3 to 5 carbon atoms, the carbocyclic ring being optionally substituted with one or more R_h;
- 40 R_h is selected from the group consisting of C1-3 alkyl, phenyl, C1-3 alkoxycarbonyl, benzyloxy and carboxy.

38. The compound according to claim 37 wherein:

5

R₁ is cyclohexyl, phenyl, naphthyl, piperidinyl, morpholinyl, piperazinyl, pyranyl, thiopyranyl or amino wherein R₁ is optionally substituted by one or more R_b;

10 R_b is selected from the group consisting of C1-3 alkyl, C5-6 cycloalkyl, phenyl, furanyl, thienyl, pyrrolyl, imidazolyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzthiazolyl, C1-3 alkoxy, C1-3 alkoxy carbonyl, carbamoyl wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, C1-5 alkanoylamino, aroylamino, C1-5 alkylsulfonylamino, 15 arylsulfonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, halogen, hydroxy, oxo, carboxy and cyano, R_b may be further optionally substituted by one or more R_c;

20 R_c is selected from the group consisting of C1-3 alkoxy, halogen and hydroxy,

R₃ is C2-5 alkyl or C5-6 cycloalkyl wherein R₃ is optionally substituted by one or more R_d;

25

R_d is selected from the group consisting of methyl, C3-6 cycloalkyl, phenyl, naphthyl, thienyl, imidazolyl, pyridinyl, indolyl, C1-4 alkoxy, C1-5 alkanoylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, halogen, hydroxy, oxo, carboxy and cyano, R_d may be further optionally substituted by one or more R_e;

30

R_e is selected from the group consisting of methyl, phenyl, benzyl, methoxy, phenoxy, benzyloxy, benzoyl, halogen and hydroxy;

35

R₆ is C1-5 alkyl or phenyl, wherein R₆ is optionally substituted by one or more R_f;

40

R_f is selected from the group consisting of C3-6 cycloalkyl, phenyl, naphthyl, thienyl, imidazolyl, pyridinyl, indolyl, methoxy, benzyloxy, C1-3 alkanoylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, methoxycarbonylamino, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, halogen, hydroxy, carboxy and cyano, R_f may be further optionally substituted by one or more R_g;

45

5 R_g is selected from the group consisting of methyl, phenyl optionally substituted by one or more groups selected from halogen or methyl, methoxy, phenoxy, benzyloxy, methoxycarbonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl or phenyl, halogen, hydroxy and carboxy;

or R₅ and R₆ together with the carbon they are attached form a carbocyclic ring of 3 to 5 carbon atoms, the carbocyclic ring being optionally substituted with one or more R_h;

10 R_h is selected from the group consisting of vinyl, phenyl, methoxycarbonyl, benzyloxycarbonyl and carboxy;

15 39. The compound according to claim 38 wherein:

R₁ is cyclohexyl, phenyl, naphthyl, piperidinyl, morpholinyl, piperazinyl, pyranyl or thiopyranyl, wherein R₁ is optionally substituted by one or more R_b;

20 R_b is selected from the group consisting of pyrrolyl, imidazolyl, indolyl, benzimidazolyl, methoxy, methoxycarbonyl, amino wherein the nitrogen atom may be independently mono or di-substituted by C1-3 alkyl, halogen, hydroxy and carboxy, R_b may be further optionally substituted by one or more R_c;

25 R_c is selected from the group consisting of methoxy, halogen and hydroxy;

30 R_d is selected from the group consisting of methyl, C3-6 cycloalkyl, phenyl, naphthyl, C1-4 alkoxy, C1-3 alkanoylamino, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, halogen, hydroxy, oxo, carboxy and cyano, R_d may be further optionally substituted by one or more R_e;

35 R_e is selected from the group consisting of methyl, phenyl, methoxy, halogen and hydroxy;

R_f is H;

40 R_f is selected from the group consisting of C5-6 cycloalkyl, phenyl, naphthyl, thienyl, indolyl, methoxy, benzyloxy, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, methoxycarbonylamino, halogen, hydroxy, carboxy and cyano, R_f may be further optionally substituted by one or more R_g;

45 R_g is selected from the group consisting of methyl, phenyl optionally substituted by halogen, methoxy, phenoxy, benzyloxy, methoxycarbonyl, halogen, hydroxy and carboxy;

or R₅ and R₆ together with the carbon they are attached form a carbocyclic ring of 3 carbon atoms, the carbocyclic ring being optionally substituted with one or more R_h;

R_h is vinyl or phenyl.

5

40. The compound according to claim 39 wherein:

10

R₁ is phenyl, naphthyl or 4-morpholinyl wherein R₁ is optionally substituted by one or more R_b;

15

R_b is selected from the group consisting of benzimidazolyl, methoxy and dimethylamino R_b may be further optionally substituted by R_c wherein R_c is a halogen atom;

20

R₃ is C2-5 alkyl wherein R₃ is optionally substituted by one or more R_d;

R_d is selected from the group consisting of C3-6 cycloalkyl, phenyl or naphthyl, R_d may be further optionally substituted by one or more R_e;

25

R_e is selected from the group consisting of methyl and halogen,

30

R_f is selected from the group consisting of C5-6 cycloalkyl, phenyl, naphthyl, indolyl, benzyloxy, methylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, benzylthio wherein the sulfur atom may be oxidized to a sulfoxide or sulfone, halogen and carboxy, R_f may be further optionally substituted by one or more R_g;

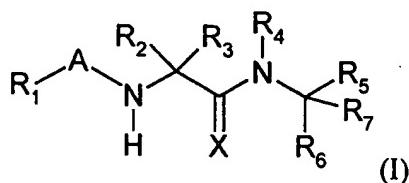
35

R_g is selected from the group consisting of methyl, methoxy, methoxycarbonyl, halogen and hydroxy, and

R₅ and R₆ together with the carbon they are attached form a carbocyclic ring of 3 carbon atoms, the carbocyclic ring being optionally substituted with one or more R_h.

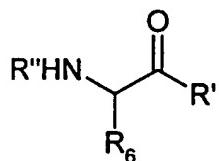
40

41. A method of making a compound of the formula(I) comprising:



wherein A is $-\text{C}(\text{O})-$, X is O, R₇ is R₈-C(O)- and R₂, R₃, R₆ and R₈ are as defined in claim 1;

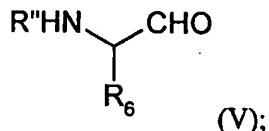
- a) coupling a protected amino acid with N,O-dimethylhydroxylamine under coupling conditions in a suitable solvent to give the corresponding amide below:



wherein R'' is an amino protecting group, R' is NM₂(OMe) and R₆ is as defined in claim 1;

10

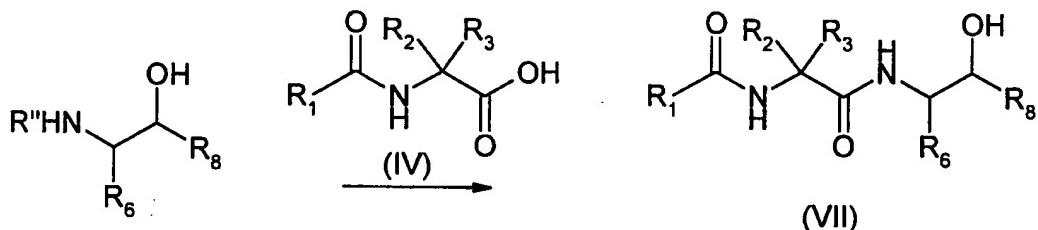
- b) reducing the compound produced in a step a) with a reducing agent in a suitable solvent to form a compound of the formula (V):



15

- d) reacting a heterocycle R₈ according to claim 1, with n-BuLi to form a corresponding heterocyclic anion in a suitable solvent at a temperature about -30 to -100 °C; reacting the heterocycle R₈ anion with a compound of formula V;

- e) removing the protecting group R" from the compound produced in step d) and subsequently coupling with a compound of the formula(IV) under coupling conditions to produce a compound of the formula (VII):



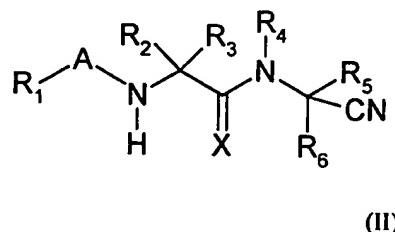
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and

- f) oxidizing compound VII from step e) to produce a compound of the formula(I).

15

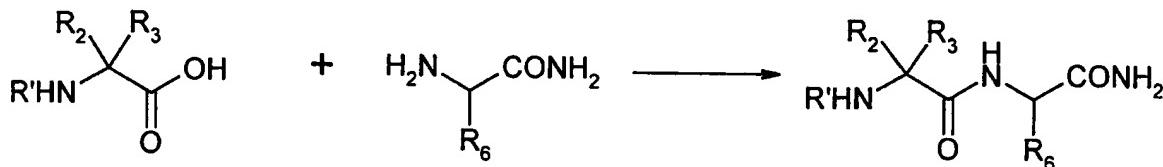
42. A method of making a compound of the formula(II) comprising:



wherein A is $-C(O)-$, X is O, and R₂, R₃, R₄, R₅ and R₆ are as defined in claim 21;

a) coupling under coupling conditions a protected amino acid with a protecting group R' with an amide compound possessing R₆:

5

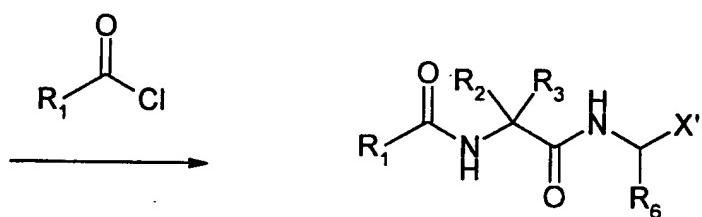


10

b) removing the protecting group R' from the compound produced in step a);

c) reacting the compound produced from step b) with an acid chloride according to the formula below:

15



wherein X' is CONH₂ and R₁ is as defined in claim 21;

and

d) dehydrating the amide compound produced in step c) with a dehydrating agent under suitable dehydrating conditions to produce the nitrile compound of the formula(II).

43. A compound selected from the group consisting of:

N-(4-morpholinecarbonyl)-L-(4-methyl)leucine (1*S*-cyano-3-phenylpropyl)amide;

5

N-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-benzyloxyethyl)amide;

N-(4-morpholinecarbonyl)-L-(4-methyl)leucine (1*R*-cyano-2-benzyloxyethyl)amide;

10 *N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2*R*-benzyloxypropyl)amide;

N-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(benzylsulfanyl)ethyl)amide;

15 *N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(2-chlorophenyl)methyloxyethyl)amide;

20 *N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(4-chlorophenyl)methyloxyethyl)amide;

N-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(3-methoxyphenyl)methyloxyethyl)amide;

25

N-(4-morpholinecarbonyl)-L-(4-methyl)leucine (1*R*-cyano-2-(benzylsulfanyl)ethyl)amide;

N-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(benzylsulfonyl)ethyl)amide;

30 *N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(benzylsulfinyl)ethyl)amide;

N-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-((4-methoxyphenyl)methylsulfanyl)ethyl)amide;

35 *N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(3-chlorophenyl)methyloxyethyl)amide;

N-(5-dimethylaminonaphth-1-ylsulfonyl)-L-leucine (1*R*-cyano-2-benzyloxyethyl)amide;

N-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(2-methylphenyl)methyloxyethyl)amide;

40

N-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(3-methylphenyl)methyloxyethyl)amide;

N-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(4-methylphenyl)methyloxyethyl)amide;

- 5 *N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(3-carbomethoxyphenyl)methyloxyethyl)amide;
- 10 5 *N*-(4-morpholinecarbonyl)-L-leucine (1*R*-cyano-2-(4-carbomethoxyphenyl)methyloxyethyl)amide;
- 15 10 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-3-(carbo-*t*-butoxy)propyl)amide;
- 20 15 10 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-3-phenylpropyl)amide;
- 25 15 15 *N*-(4-Morpholinecarbonyl)-L-leucine-[1*S*(benzthiazol-2-ylcarbonyl)-3-phenylpropyl]amide;
- 30 20 20 *N*-(4-morpholinecarbonyl)-L-leucine [[1-[(6-phenylcarbamoyl)benzothiazol-2-ylcarbonyl]-3-phenylpropyl]]amide;
- 35 25 25 *N*-(4-Morpholinecarbonyl)-L-leucine-[[6-(carbomethoxy)-benzoxazol-2-ylcarbonyl]-3-phenylpropyl]amide;
- 40 30 30 *N*-(4-morpholinecarbonyl)-L-cyclohexylalanine (1*S*-cyano-3-phenylpropyl)amide;
- 45 35 35 *N*-(4-morpholinecarbonyl)-L-cyclohexylalanine (1*R*-cyano-2-benzyloxyethyl)amide;
- 50 40 40 *N*-(4-morpholinecarbonyl)-L-nor-leucine (1*S*-cyano-3-phenylpropyl)amide;
- 55 45 45 *N*-(4-Morpholinecarbonyl)-L-leucine 1*RS*-((5-phenyloxazol-2-yl)carbonyl)-3-phenylpropylamide;
- 60 50 50 *N*-(4-Morpholinecarbonyl)-L-leucine 1*S*-(oxazol-2-ylcarbonyl)-3-phenylpropylamide;
- 65 55 55 *N*-(4-morpholinecarbonyl)-L-(4-methyl)leucine [1-(Benzothiazol-2-ylcarbonyl)-3-phenylpropyl]amide;
- 70 60 60 *N*-(4-morpholinecarbonyl)-L-(2-naphthyl)alanine (1*S*-cyano-3-phenylpropyl)amide;
- 75 65 65 *N*-(4-morpholinecarbonyl)-L-(2-chlorophenyl)alanine (1*S*-cyano-3-phenylpropyl)amide;
- 80 70 70 *N*-Benzoyl-L-leucine (1*R*-cyano-2-benzyloxyethyl)amide;

- N*-(4-morpholinecarbonyl)-L-(O-methyl)tyrosine (1*S*-cyano-3-phenylpropyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine(1*S*-cyano-2-(carbobenzyloxy)ethyl)amide;
- 5 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-1-phenylmethyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1-cyanocyclopropyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(2-chlorophenyl)ethyl)amide;
- 10 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-(4-(2,6-dichloromethoxy)phenyl)ethyl)amide;
- 15 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-3-(carbobenzyloxy)propyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*S*,3-dicyanopropyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*S*,2-dicyanoethyl)amide;
- 20 *N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-3-(methylsulfonyl)propyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-3-(4-hydroxyphenyl)propyl)amide;
- N*-(4-morpholinecarbonyl)-L-leucine (1*S*-cyano-2-cyclohexylethyl)amide and
- 25 pharmaceutically acceptable derivatives thereof.

44. A compound selected from the group consisting of:

- 30 Morpholine-4-carboxylic acid {1-(*S*)-[1(*S*)-(2,4-diphenyl-oxazole-5-carbonyl)-3-phenyl-propylcarbamoyl]-3,3-dimethylbutyl} amide;
- Morpholine-4-carboxylic acid {2-cyclohexyl-1-(*S*)-[1-(*S*)-(2,4-diphenyl-oxazole-5-carbonyl)-3-phenyl-propylcarbamoyl]-ethyl} amide;
- 35 Morpholine-4-carboxylic acid {1-(*S*)-[2,4-diphenyl-oxazole-5-yl]-2-oxo-ethylcarbamoyl]-3-methylbutyl} amide;
- Morpholine-4-carboxylic acid {2-cyclohexyl-1-(*S*)-[2-(2,4-diphenyl-oxazol-5-yl)-2-oxo-ethylcarbamoyl]-ethyl}-amide;

40

- Morpholine-4-carboxylic acid {1-(*S*)-[2-(2,4-diphenyl-oxazol-5-yl)-2-oxoethylcarbamoyl]-3,3-dimethylbutyl}-amide;
- 5 Morpholine-4-carboxylic acid (1-(*S*)-{1-(*S*)-[2-(3-benzyloxy-phenyl)-oxazole-5-carbonyl]-3-phenyl-propylcarbamoyl}-3-methyl-butyl)-amide;
- Morpholine-4-carboxylic acid {2-cyclohexyl-1-(*S*)-[1-(*R,S*)-(4-isobutyl-2-pyrinin-2-yl-oxazole-5-carbonyl)-3-phenyl-propylcarbamoyl]-ethyl} amide and
- 10 the pharmaceutically acceptable derivatives thereof.
45. A pharmaceutical composition comprising a pharmaceutically effective amount of a compound according to claims 1, 11, 21, 31 or 43.
- 15
46. A method of modulating an autoimmune disease, said method comprising administering to a patient in need of such treatment a pharmaceutically effective amount of a compound according to claims 1, 11, 21, 31 or 43.
- 20 47. The method according to claim 46 wherein the autoimmune disease is selected from the group consisting of: rheumatoid arthritis, systemic lupus erythematosus, Crohn's disease, ulcerative colitis, multiple sclerosis, Guillain-Barre syndrome, psoriasis, Grave's disease, myasthenia gravis, scleroderma, glomerulonephritis, atopic dermatitis and insulin-dependent diabetes mellitus.
- 25
48. A method of treating Alzheimer's disease comprising administering to a patient in need of such treatment a pharmaceutically effective amount of a compound according to claims 1, 11, 21, 31 or 43.

49. A method of treating atherosclerosis comprising administering to a patient in need of such treatment a pharmaceutically effective amount of a compound according to claims 1, 11, 21, 31 or 43.

INTERNATIONAL SEARCH REPORT

Int. Jonal Application No
PCT/US 99/26278

A. CLASSIFICATION OF SUBJECT MATTER					
IPC 7	C07D277/64	C07D263/32	C07D413/04	C07D295/20	C07C311/42
	A61P9/10	A61P25/28	A61P37/02		

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07D C07C A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>CHEMICAL ABSTRACTS, vol. 113, no. 21, 19 November 1990 (1990-11-19) Columbus, Ohio, US; abstract no. 187051, HANZLIK, ROBERT P. ET AL: "Reversible covalent binding of peptide nitriles to papain" XP002129208 cited in the application abstract & BIOCHIM. BIOPHYS. ACTA (1990), 1035(1), 62-70 , ----</p> <p style="text-align: center;">-/-</p>	21-49

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

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Date of the actual completion of the international search

28 January 2000

Date of mailing of the international search report

14/02/2000

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INTERNATIONAL SEARCH REPORT

International Application No

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	CHEMICAL ABSTRACTS, vol. 102, no. 1, 7 January 1985 (1985-01-07) Columbus, Ohio, US; abstract no. 2545, CAREY, PAUL R. ET AL: "Identity of acyl group conformations in the active sites of papain and cathepsin B by resonance Raman spectroscopy" XP002129209 abstract & J. BIOL. CHEM. (1984), 259(23), 14357-60 ,	21-49
X	DUFOUR, ERIC ET AL: "Engineering nitrile hydratase activity into a cysteine protease by a single mutation" BIOCHEMISTRY (1995), 34(50), 16382-8 , XP002129204 page 16384 -page 16387 ---	21-49
X	CHEMICAL ABSTRACTS, vol. 120, no. 23, 6 June 1994 (1994-06-06) Columbus, Ohio, US; abstract no. 292661, LIU, SIMING ET AL: "The contribution of intermolecular hydrogen bonding to the kinetic specificity of papain" XP002129210 abstract & BIOCHIM. BIOPHYS. ACTA (1993), 1158(3), 264-72 , ---	21-49
X	GOUR-SALIN, BARBARA J. ET AL: "Inhibition of papain by peptide nitriles: conversion of the nitrile group into other functionalities via the papain:nitrile thioimide ester adduct" CAN. J. CHEM. (1991), 69(8), 1288-97 , XP002129205 cited in the application page 1289 -page 1291 ---	21-49
X	CHEMICAL ABSTRACTS, vol. 113, no. 21, 19 November 1990 (1990-11-19) Columbus, Ohio, US; abstract no. 187051, HANZLIK, ROBERT P. ET AL: "Reversible covalent binding of peptide nitriles to papain" XP002129211 cited in the application abstract & BIOCHIM. BIOPHYS. ACTA (1990), 1035(1), 62-70 , ---	21-49

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INTERNATIONAL SEARCH REPORT

Int	tional Application No
PCT/US 99/26278	

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	CHEMICAL ABSTRACTS, vol. 111, no. 15, 9 October 1989 (1989-10-09) Columbus, Ohio, US; abstract no. 129491, BUTTLE, DAVID J. ET AL: "Affinity purification of the novel cysteine proteinase papaya proteinase IV, and papain from papaya latex" XP002129212 abstract & BIOCHEM. J. (1989), 261(2), 469-76 , ---	21-49
X	CHEMICAL ABSTRACTS, vol. 107, no. 1, 6 July 1987 (1987-07-06) Columbus, Ohio, US; abstract no. 3097, LIANG, TZYY CHYAU ET AL: "Inhibition of papain by nitriles: mechanistic studies using NMR and kinetic measurements" XP002129213 abstract & ARCH. BIOCHEM. BIOPHYS. (1987), 252(2), 626-34 , ---	21-49
X	MOON, JOSEPH B. ET AL: "Reversible covalent inhibition of papain by a peptide nitrile. Carbon-13 NMR evidence for a thioimidate ester adduct" J. AM. CHEM. SOC. (1986), 108(6), 1350-1 , XP002129206 the whole document ---	21-49
X	ASBOTH, BENCE ET AL: "Mechanism of action of cysteine proteinases: oxyanion binding site is not essential in the hydrolysis of specific substrates" BIOCHEMISTRY (1985), 24(3), 606-9 , XP002129207 page 607 ---	21-49
X	WO 92 17453 A (DU PONT MERCK PHARMA) 15 October 1992 (1992-10-15) * see the examples * ---	21-49
X	WO 95 24382 A (SEARLE & CO ;HALLINAN E ANN (US); TJOENG FOE S (US); FOK KAM F (US) 14 September 1995 (1995-09-14) the whole document ---	21-49
X	WO 97 27220 A (BASF AG ;PARKE DAVIS (US)) 31 July 1997 (1997-07-31) page 11-12 ---	21-49
	-/-	

INTERNATIONAL SEARCH REPORT

Int. & dom. Application No.

PCT/US 99/26278

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 95 09838 A (MERRELL DOW PHARMA ; SCOIS NOVA INC (US); CORDELL BARBARA (US); SCH) 13 April 1995 (1995-04-13) * see the examples * ---	1
A	WO 95 15749 A (PROTOTEK INC) 15 June 1995 (1995-06-15) * see the claims and the examples * ---	1
A	WO 96 40647 A (PROTOTEK INC) 19 December 1996 (1996-12-19) * see the examples * ---	1
A	US 5 691 368 A (PEET NORTON P ET AL) 25 November 1997 (1997-11-25) * see the examples * ---	1
P,X	WO 99 24460 A (NOVARTIS ERFINDUNGEN VERWALTUNG ; ALTMANN EVA (CH); LATTMANN RENE (C) 20 May 1999 (1999-05-20) * see the examples * abstract; claim 1 -----	1-49

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Present claims 1-42, 45-49 relate to an extremely large number of possible compounds. Support within the meaning of Article 6 PCT and disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the compounds claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to the compounds as displayed by formula (I) on page 175, wherein R1 is a 4-morpholino substituent, and compounds as displayed by formula (II) on page 247, the compounds as mentioned in the description on pages 129-146, the examples on pages 157-167 and the "prophetic" compounds on pages 171 and 174.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members			International Application No PCT/US 99/26278	
Patent document cited in search report	Publication date	Patent family member(s)		Publication date
WO 9217453	A 15-10-1992	US AU AU CZ EP EP FI HU IL JP MX NO NZ SK RU US US ZA LV	5206249 A 666847 B 1767692 A 9302060 A 0506008 A 0577753 A 934225 A 68969 A 101380 A 6506229 T 9201355 A 933455 A, B, 242126 A 107193 A 2066316 C 5329048 A 5461176 A 9202252 A 10045 A, B	27-04-1993 29-02-1996 02-11-1992 16-03-1994 30-09-1992 12-01-1994 15-10-1993 28-08-1995 31-10-1996 14-07-1994 01-10-1992 26-11-1993 25-09-1996 10-08-1994 10-09-1996 12-07-1994 24-10-1993 27-09-1993 10-05-1994
WO 9524382	A 14-09-1995	AU CA EP	2115695 A 2184691 A 0749418 A	25-09-1995 14-09-1995 27-12-1996
WO 9727220	A 31-07-1997	AU CA EP	2114197 A 2243497 A 0880542 A	20-08-1997 31-07-1997 02-12-1998
WO 9509838	A 13-04-1995	AU AU CA CN EP FI HU IL JP NO NZ US ZA	687449 B 7799894 A 2171882 A 1132504 A 0721449 A 961438 A 74004 A 111078 A 9505281 T 961326 A 274074 A 5977074 A 9407529 A	26-02-1998 01-05-1995 13-04-1995 02-10-1996 17-07-1996 29-03-1996 28-10-1996 12-03-1999 27-05-1997 01-04-1996 24-11-1997 02-11-1999 29-05-1995
WO 9515749	A 15-06-1995	US AU CA EP JP US US US	5486623 A 1266495 A 2177495 A 0731696 A 9506368 T 5714484 A 5663380 A 5925772 A	23-01-1996 27-06-1995 15-06-1995 18-09-1996 24-06-1997 03-02-1998 02-09-1997 20-07-1999
WO 9640647	A 19-12-1996	US AU AU CA EP JP	5714484 A 713934 B 6100996 A 2223268 A 0863883 A 11507912 T	03-02-1998 16-12-1999 30-12-1996 19-12-1996 16-09-1998 13-07-1999

INTERNATIONAL SEARCH REPORT

Information on patent family members			International Application No PCT/US 99/26278	
Patent document cited in search report	Publication date	Patent family member(s)		Publication date
US 5691368	A	25-11-1997	AU 692044 B AU 4473196 A CA 2210258 A CN 1173174 A EP 0802909 A FI 972935 A HU 77649 A JP 10512257 T NO 973216 A NZ 298999 A WO 9621655 A ZA 9600100 A	28-05-1998 31-07-1996 18-07-1996 11-02-1998 29-10-1997 10-07-1997 28-07-1998 24-11-1998 09-09-1997 28-01-1999 18-07-1996 24-07-1996
<hr/> WO 9924460	A	20-05-1999	AU 1487399 A	31-05-1999

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